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8D14

SEARCH REQUEST FORM

Requestor's Name: L. E. Crane

Serial Number: 8 08/648,270

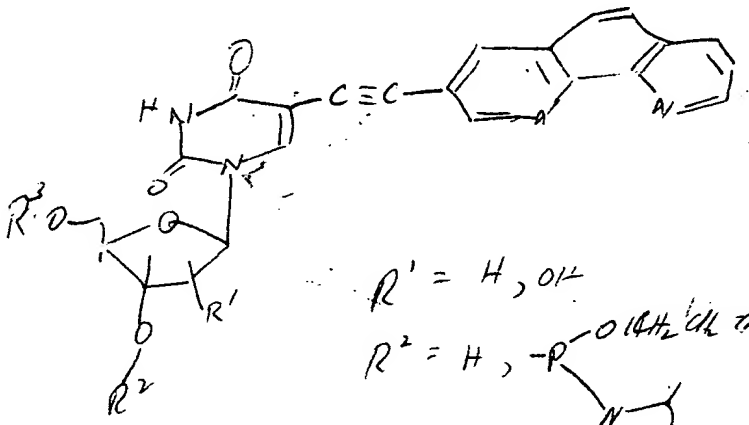
6-365

Date: 06/10/98 Phone: 308-4639 Art Unit: 1623

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

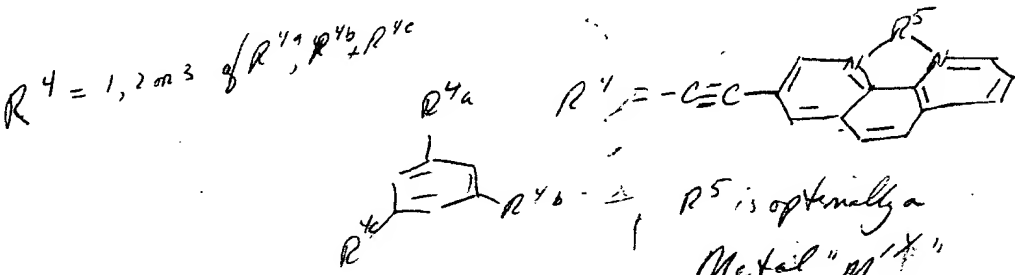
Please search the following structures



R^1 = H, OH

R^2 = H, $-P(OCH_2CH_2CN)N$

R^3 = H, $-PO_3^=$



R^4 = 1, 2 or 3 of R^{4a}, R^{4b}, R^{4c}

R^1 = $-C\equiv C-$

R^5 is optionally a Metal "M" selected from group Cd, Cu, Co, Zn, Fe, Ru, Rh, Os, Re;

03:9 M 11 [illegible]

STAFF USE ONLY

Date completed: 6/17/98 308-4290

Searcher: Kathleen Fuller RM 1E01

Terminal time: 23

Elapsed time:

CPU time:

Total time: 35

Number of Searches:

Number of Databases:

Search Site

- ____ STIC
- ____ CM-1
- ____ Pre-S

Type of Search

- ____ N.A. Sequence
- ____ A.A. Sequence
- ____ Structure
- ____ Bibliographic

Vendors

- ____ IG
- ____ STN
- ____ Dialog
- ____ APS
- ____ Geninfo
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- ____ DARC/Questel
- ____ Other

PTO-1590 (9-90)

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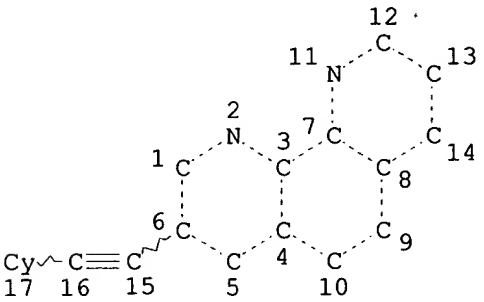
FILE COVERS 1967 - 17 Jun 1998 VOL 128 ISS 25
FILE LAST UPDATED: 17 Jun 1998 (980617/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file now supports REG1stRY for direct browsing and searching of all non-structural data from the REGISTRY file. Enter HELP FIRST for more information.

=> D QUE L68
L65 STR



← query covers both structures

66 structures found

↓

8 CA ref's
zero CoOld ref's

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L67 66 SEA FILE=REGISTRY SSS FUL L65
L68 8 SEA FILE=HCAPLUS ABB=ON L67

=> D L68 1-8 CBIB ABS IND HITSTR

L68 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1998:150247 Document No. 128:192875 Metal-Containing Oligonucleotides: Solid-Phase Synthesis and Luminescence Properties. Hurley, Dennis J.; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA, 92093-0358, USA). J. Am. Chem. Soc., 120(9), 2194-2195 (English) 1998. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CJACS-IMAGE; CJACS. Publisher: American Chemical Society.

AB A general and versatile method for the site-specific incorporation of polypyridine RuII and OsII complexes into DNA oligonucleotides using automated solid-phase phosphoramidite chem. is reported. The novel phosphoramidites contg. a [(bpy)2M(3-ethynyl-1,10-phenanthroline)]2+ (M = Ru, Os) metal center covalently attached to the 5-position in 2'-deoxyuridine are synthesized and utilized for high yield synthesis of metal-modified oligodeoxyribonucleotides. The novel oligonucleotides, characterized by absorption and fluorescence spectroscopy, enzymic digestion and electrophoresis, form stable duplexes and are useful probes for the study of energy-transfer processes in nucleic acids.

CC 33-10 (Carbohydrates)
Section cross-reference(s): 22, 78

ST ethynyldeoxyuridine coupling palladium catalyst rutheniumphenanthroline luminescence; DNA duplex metal contg synthesis luminescence; osmium complex oligodeoxyribonucleotide synthesis luminescence; luminescence ruthenium complex oligodeoxyribonucleotide duplex synthesis; solid phase synthesis metal contg oligodeoxyribonucleotide

IT Luminescence
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

IT DNA
Oligodeoxyribonucleotides
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

IT 203461-41-0P 203461-42-1P 203461-43-2P 203461-44-3P
203461-45-4P 203461-46-5P 203461-47-6P 203461-48-7P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

IT 61135-33-9 178314-93-7 201653-01-2
RL: RCT (Reactant)
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

IT 117626-97-8P **203382-81-4P 203382-83-6P**
203382-85-8P 203382-87-0P 203382-89-2P
203382-91-6P 203461-35-2P 203461-36-3P 203461-37-4P
203461-38-5P 203461-39-6P 203461-40-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

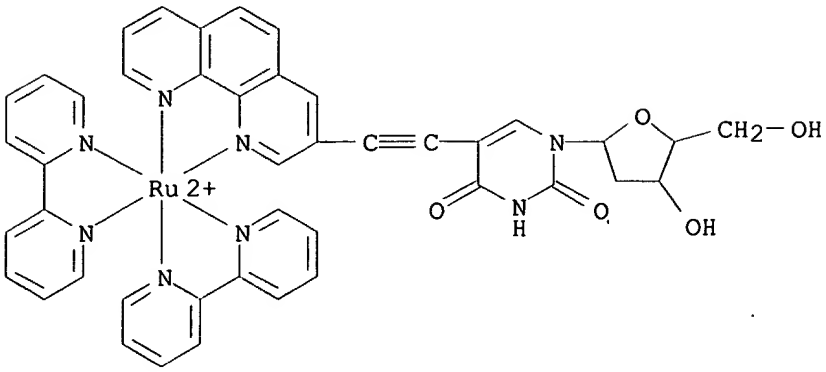
IT **203382-81-4P 203382-83-6P 203382-85-8P**
203382-87-0P 203382-89-2P 203382-91-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis and luminescence properties of metal-contg. oligodeoxyribonucleotides)

RN 203382-81-4 HCAPLUS

CN Ruthenium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

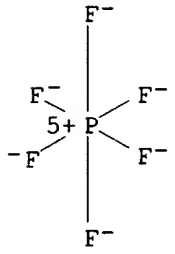
CM 1

CRN 203382-80-3
CMF C43 H34 N8 O5 Ru
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



RN 203382-83-6 HCAPLUS
CN Osmium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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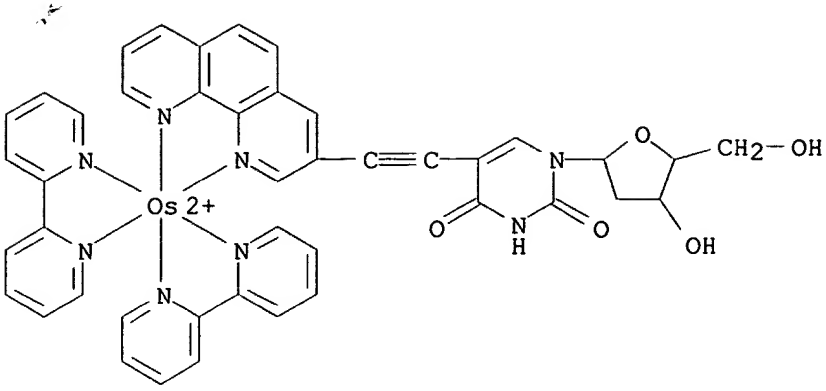
CRN 203382-82-5
CMF C43 H34 N8 O5 Os
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)



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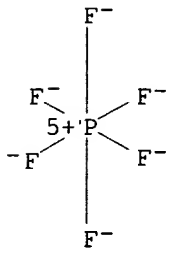
CRN 16919-18-9
CMF F6 P
CCI CCS

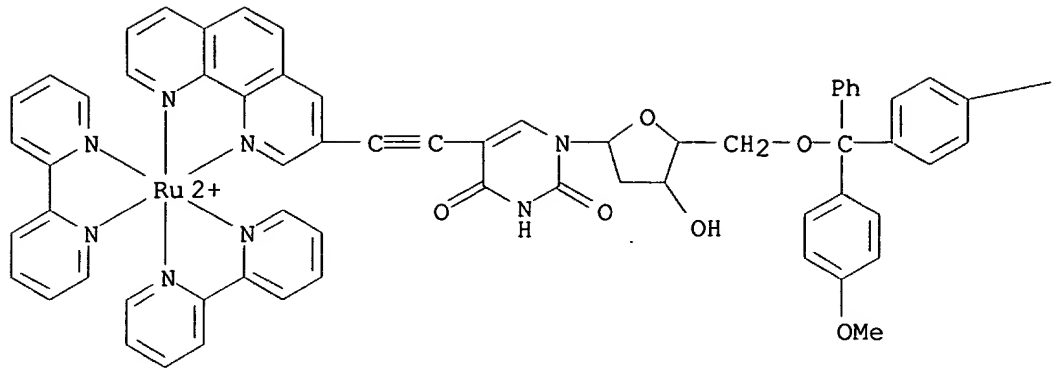


RN 203382-85-8 HCAPLUS
CN Ruthenium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 203382-84-7
CMF C64 H52 N8 O7 Ru
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)

PAGE 1-A

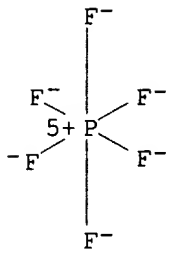


PAGE 1-B

— OMe

CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

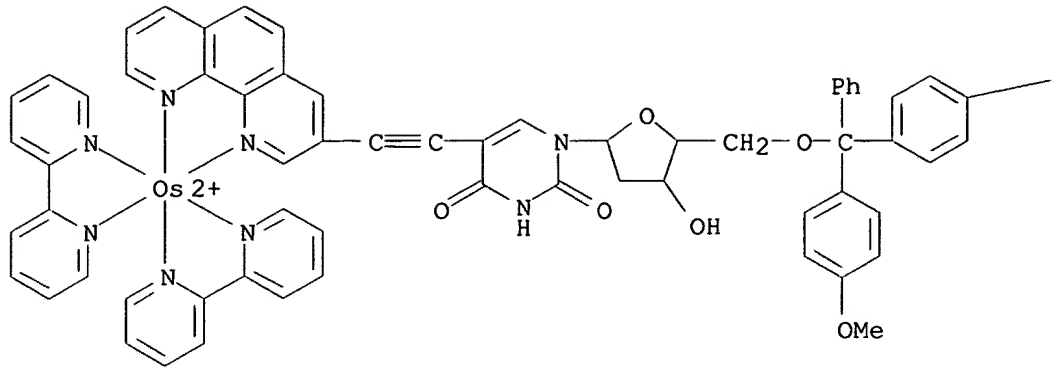


RN 203382-87-0 HCAPLUS
CN Osmium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 203382-86-9
CMF C64 H52 N8 O7 Os
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)

PAGE 1-A

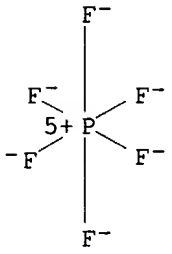


PAGE 1-B

— OMe

CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



RN 203382-89-2 HCAPLUS
CN Ruthenium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite]]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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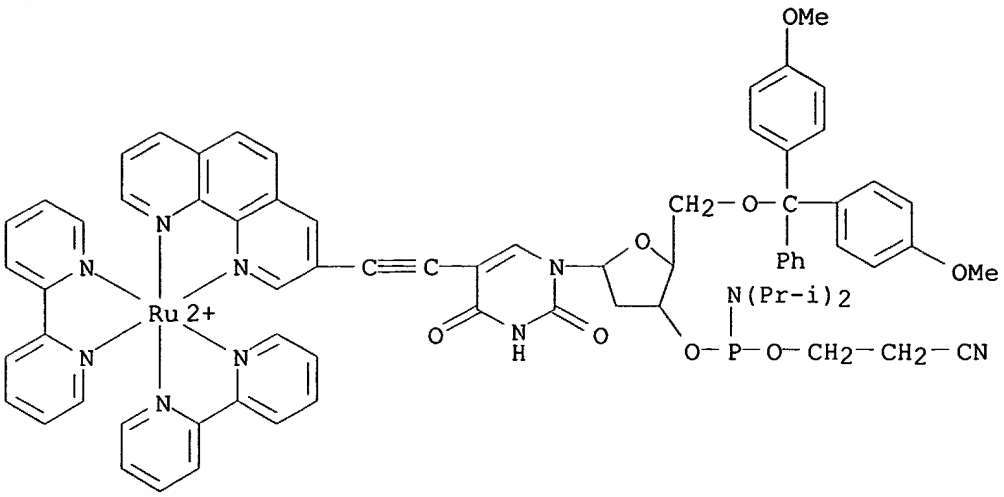
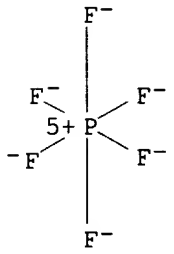
CRN 203382-88-1
CMF C73 H69 N10 O8 P Ru
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)



CM 2

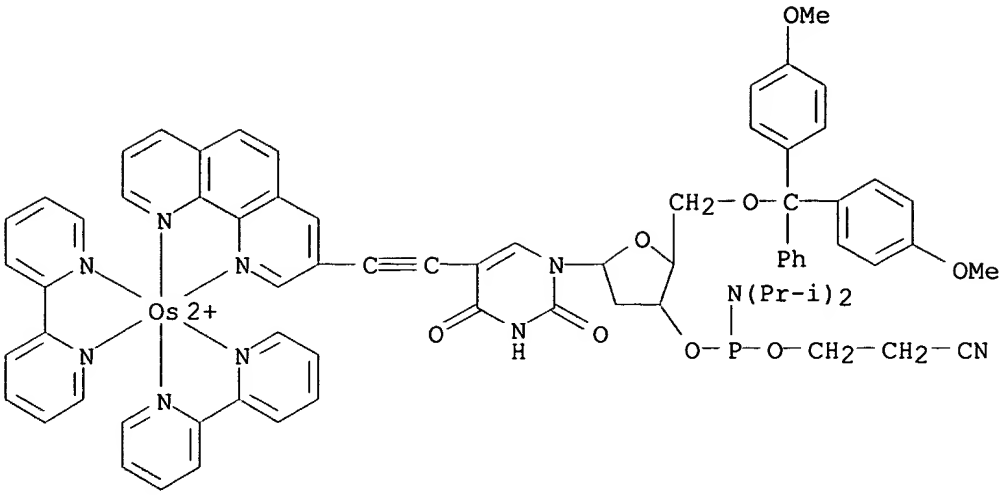
CRN 16919-18-9
CMF F6 P
CCI CCS



RN 203382-91-6 HCAPLUS
CN Osmium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-5-[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]uridine 3'-[2-cyanoethyl bis(1-methylethyl)phosphoramidite]]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

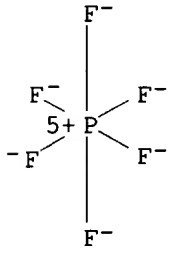
CM 1

CRN 203382-90-5
CMF C73 H69 N10 O8 Os P
CCI CCS
CDES 7:OC-6-33.(B-D-ERYTHRO)



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1998:112952 Document No. 128:175283 Coordination Compounds as Building Blocks: Single-Step Synthesis of Heteronuclear Multimetallic Complexes Containing RuII and OsII. Connors, Patrick J., Jr.; Tzalis, Dimitrios; Dunnick, Alejandro L.; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California at San Diego, La Jolla, CA, 92093-0358, USA). Inorg. Chem., 37(5), 1121-1123 (English) 1998. CODEN: INOCAJ. ISSN: 0020-1669. OTHER SOURCES: CJACS-IMAGE; CJACS. Publisher: American Chemical Society.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB I(PF6)4 (M = M' = Ru; M = Ru, M' = Os; M = M' = Os) and II(PF6)6 (M = Ru, M' = Os; M = Os, M' = Ru) were prepd. via Pd-catalyzed cross coupling reactions of bromo- and ethynyl-functionalized Ru(II) and Os(II) complexes. MLCT spectra are discussed for the mononuclear reactants and the polynuclear products. I show reversible oxidn. couples with the heterodinuclear complex showing sep. processes at +1.02 and +0.58 for the Ru(II)/(III) and Os(II)/(III) centers vs.

Ag/Ag+. This synthesis demonstrates a simple, direct method of prepg. polynuclear materials.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 28, 72, 73

ST ruthenium osmium bipyridine ethynylphenanthroline polynuclear prepn; coupling ruthenium osmium bipyridine ethynylphenanthroline polynuclear; redox ruthenium osmium bipyridine ethynylphenanthroline polynuclear; ethynyl linked ruthenium osmium phenanthroline polynuclear

IT Redox potential
(of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

IT Cross-coupling reaction
(of ruthenium and osmium bipyridine complexes with bromo- and ethynyl-substituted phenanthrolines)

IT 72287-26-4, [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium
RL: CAT (Catalyst use); USES (Uses)
(catalyst for prepn. of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

IT **202601-16-9 202601-21-6 202601-22-7**
202601-23-8
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(elec. potential of couple contg.)

IT 178314-93-7P 178314-95-9P 201653-01-2P 202601-03-4P
202601-05-6P 202601-07-8P 202667-34-3P 202667-36-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

IT 66-71-7, 1,10-Phenanthroline 15702-72-4 15746-57-3
178315-04-3, 3-Ethynyl-1,10-phenanthroline
RL: RCT (Reactant)
(for prepn. of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

IT 66127-01-3P, 3-Bromo-1,10-phenanthroline 100125-12-0P,
3,8-Dibromo-1,10-phenanthroline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

IT 202601-18-1P 202601-20-5P
RL: BYP (Byproduct); PREP (Preparation)
(in prepn. of ethynyl-linked ruthenium osmium bipyridine phenanthroline homo- and heteropolynuclear complexes)

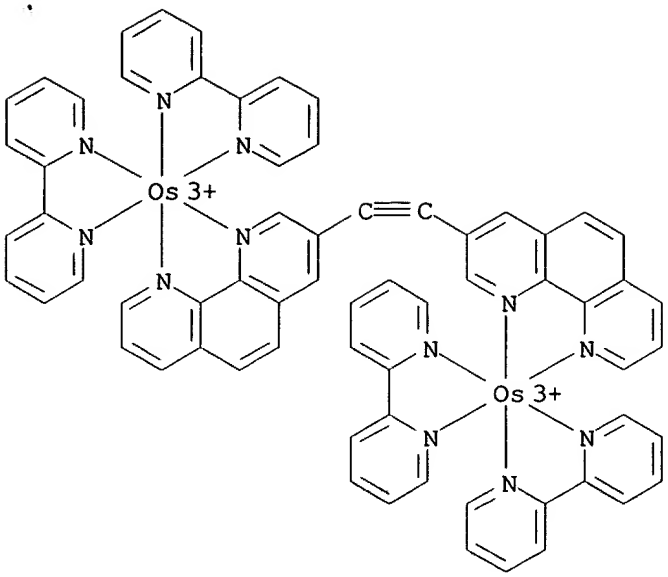
IT **202601-13-6P 202601-15-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn., MLCT spectra and cyclic voltammetry of)

IT **202601-09-0P 202601-11-4P 202802-38-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn., MLCT spectra and redox potential of)

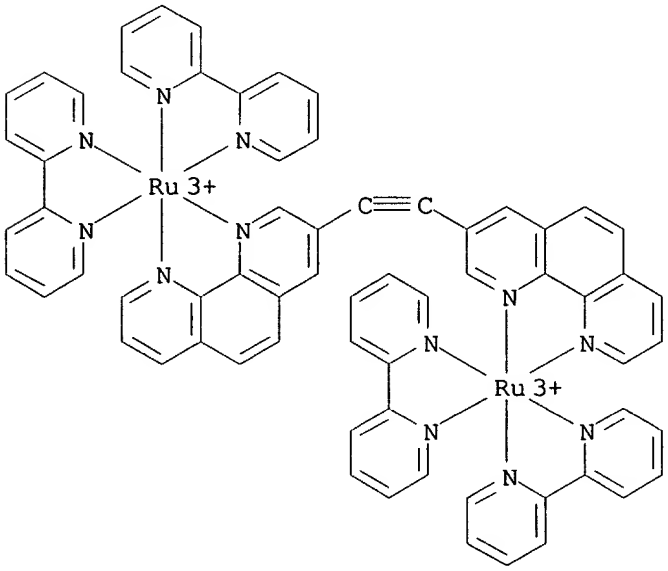
IT **202601-16-9 202601-21-6 202601-22-7**
202601-23-8
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(elec. potential of couple contg.)

RN 202601-16-9 HCAPLUS

CN Osmium(6+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di- (9CI) (CA INDEX NAME)



RN 202601-21-6 HCAPLUS
CN Ruthenium(6+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di- (9CI) (CA INDEX NAME)

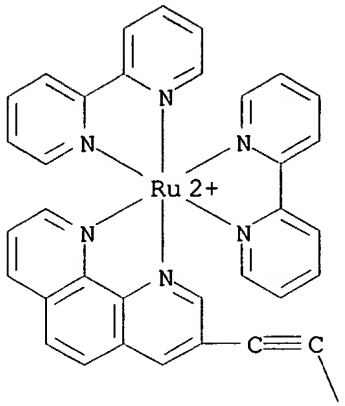


RN 202601-22-7 HCAPLUS
CN Osmium(5+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')ruthenium]operties); SPN (Synthetic preparation);
PREP
(Preparation)
(prepn., MLCT spectra and cyclic voltammetry of)
RN 202601-13-6 HCAPLUS
CN Osmium(6+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')bis[bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')ruthenium][.mu.3-[3,8-bis[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]]-, hexakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

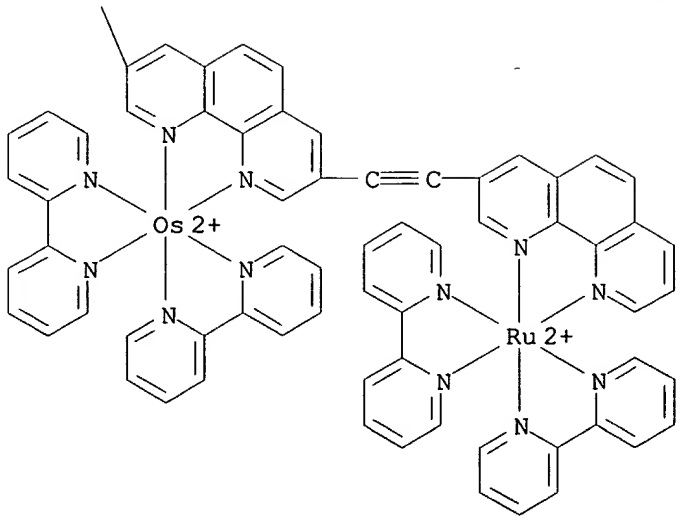
CM 1

CRN 202601-12-5
CMF C100 H68 N18 Os Ru2
CCI CCS

PAGE 1-A



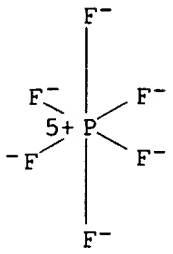
PAGE 2-A



CM 2

CRN 16919-18-9
CMF F6 P

CCI CCS



RN 202601-15-8 HCAPLUS
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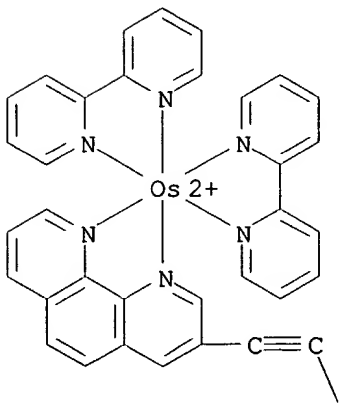
CM 1

CRN 202601-14-7
CMF C100 H68 N18 Os2 Ru
CCI CCS

PAGE 1-A



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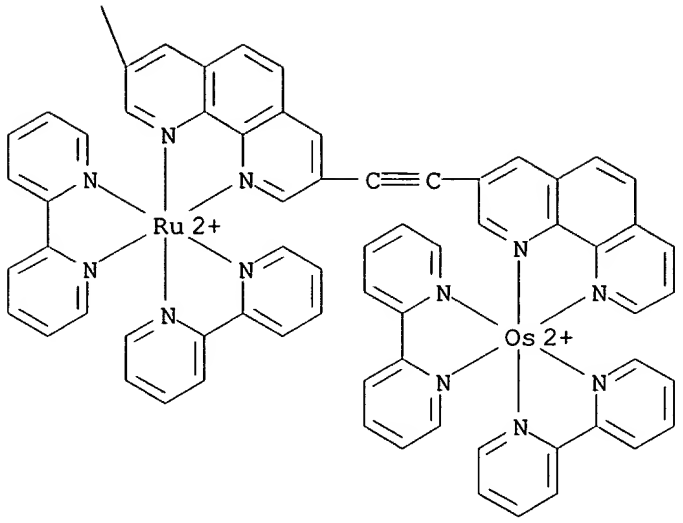

CM 2

CRN 16919-18-9
CMF F6 P
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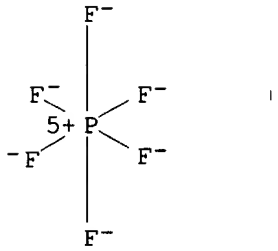

IT **202601-09-0P 202601-11-4P 202802-38-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn., MLCT spectra and redox potential of)
RN 202601-09-0 HCAPLUS
CN Osmium(4+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')ruthenium][.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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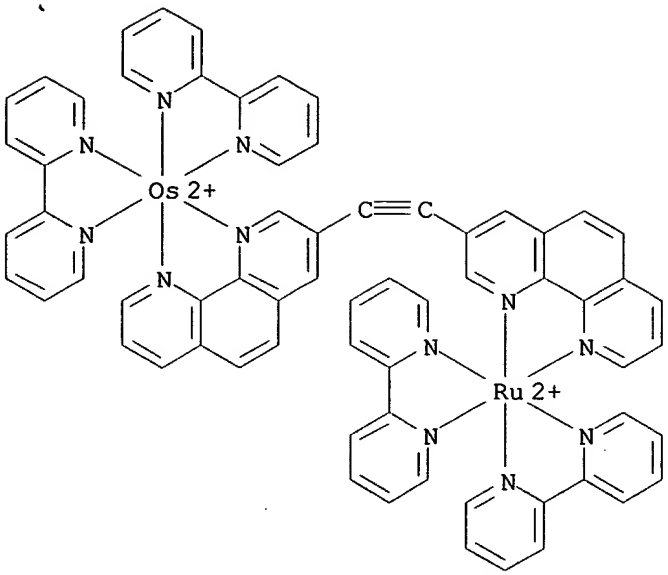
CRN 202601-08-9
CMF C66 H46 N12 Os Ru
CCI CCS



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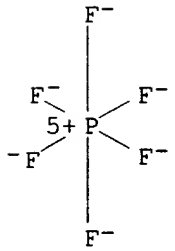
CRN 16919-18-9
CMF F6 P
CCI CCS



RN 202601-11-4 HCAPLUS
CN Osmium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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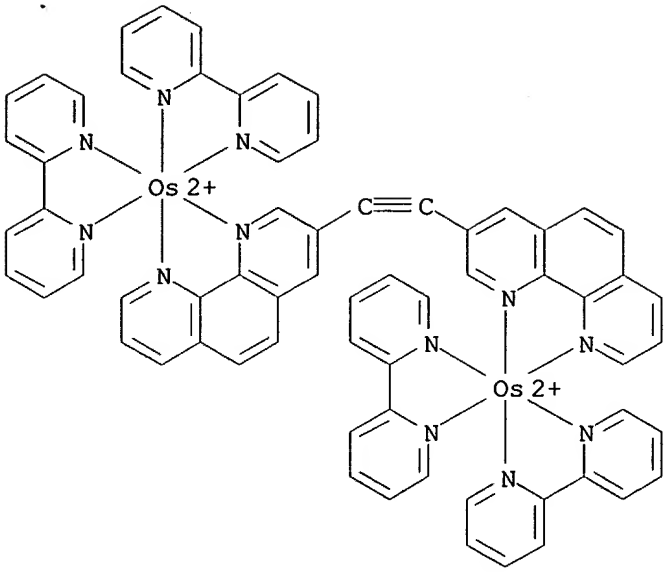
CCI CCS



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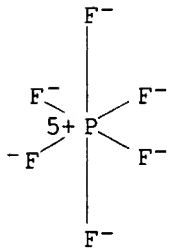
CRN 16919-18-9
CMF F6 P
CCI CCS



RN 202802-38-8 HCAPLUS
CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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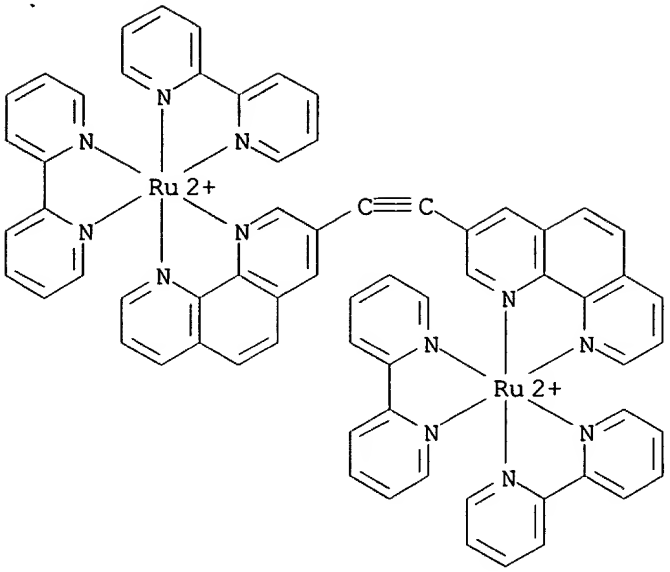
CRN 202802-37-7
CMF C66 H46 N12 Ru2
CCI CCS



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CMF F6 P
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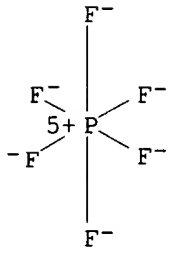
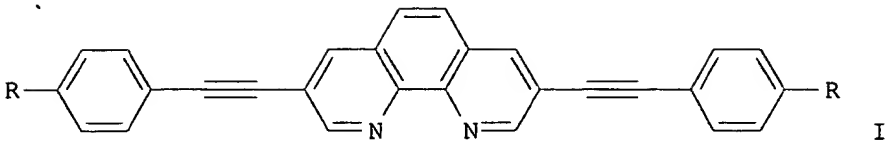
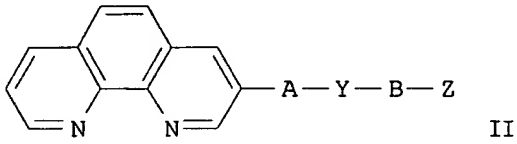


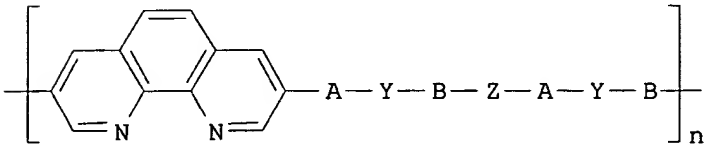
L68 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1997:740229 Document No. 128:9803 Preparation of 3- and 3,8-substituted 1,10-phenanthrolines and their transition metal complexes for use in electron and energy transfer processes. Tor, Yitzhak; Tzalis, Dimitrios (Regents of the University of California, USA; Tor, Yitzhak; Tzalis, Dimitrios). PCT Int. Appl. WO 9741122 A1 971106, 38 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 97-US7259 970429. PRIORITY: US 96-16575 960430; US 96-648270 960515.
GI



I



II



III

AB The invention relates to the prepn. of 1,10-phenanthroline derivs. substituted at the 3- or 3,8-positions, their transition metal complexes, and their use in electron and energy transfer processes. A method for prepg. 1,10-phenanthrolines substituted at the 3,8-positions with acetylene derivs. (preferably arom. acetylenes) is claimed. In an example, bromination of 1,10-phenanthroline monohydrochloride monohydrate in nitrobenzene (or bromobenzene) solvent occurs regioselectively to afford 3-bromo-1,10-phenanthroline and 3,8-dibromo-1,10-phenanthroline. Cross-coupling reactions between 3,8-dibromo-1,10-phenanthroline and (un)substituted phenylacetylenes, e.g., 4-RC6H4C.tplbond.CH (R = H, Me, OMe, CF3), in MeOH in the presence of (Ph3P)2PdCl2 and CuI with added Et3N and with sonication afforded corresponding 3,8-phenylethynyl derivs. I. Hydrogenation of the above acetylene derivs. to form alkene or alkane derivs. of 1,10-phenanthroline is also claimed (no examples). Transition metal complexes contg. the chelated 3,8-ethynyl derivs. of 1,10-phenanthroline are claimed. Also claimed are 3-substituted 1,10-phenanthrolines, e.g., II [A, B = C or N; Y = C.tplbond.C, alkenediyl, alkanediyl, azo, imino; Z = (un)substituted alkyl, (un)substituted arom. group], or their polymers III, and their chelate complexes with transition metals. Oligomeric complexes IV (Z = preferably arom. group, e.g., tri-substituted C6H3; M = metal ion; X, X1 = co-ligands) are also claimed. The Pd-mediated cross-coupling reactions described are preferably done with the compds. already contg. the transition metal ions and co-ligands. This has the advantage of prepg. diastereomerically pure metal-contg. Z compds. wherein Z comprises the base of a nucleoside or nucleotide, the phosphoramidite form of the nucleotide, or a nucleic acid. The prepd. compds. are useful in a wide variety of applications related to electron and energy transfer processes.

IC ICM C07D471-04
ICS C07H019-23; G01N033-533
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 28, 33, 34, 73
ST phenanthroline phenylethynyl prepn complexation transition metal; bromophenanthroline regioselective prepn cross coupling ethynylbenzene; regioselective bromination phenanthroline; transition metal phenanthroline phenylethynyl linked prepn; nucleoside transition metal phenanthroline ethynyl linked; nucleotide transition metal phenanthroline ethynyl linked; nucleic

acid metal phenanthroline ethynyl linked; polymer transition metal phenanthroline ethynyl linked; hydrogenation ethynylphenanthroline ligand; dendrimer ethynylphenanthroline transition metal prepn

IT Nucleic acids
RL: SPN (Synthetic preparation); PREP (Preparation)
(ethynyl-linked phenanthroline derivs.; prepn. of nucleic acids linked to 1,10-phenanthroline ligand via ethynyl group(s) in the 3- and 3,8-positions of 1,10-phenanthroline)

IT Nucleosides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(ethynyl-linked phenanthroline derivs.; prepn. of nucleosides linked to 1,10-phenanthroline ligand via ethynyl group(s) in the 3- and 3,8-positions of 1,10-phenanthroline)

IT Nucleotides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(ethynyl-linked phenanthroline derivs.; prepn. of nucleotides and phosphoramidite derivs. linked to 1,10-phenanthroline ligand via ethynyl group(s) in the 3- and 3,8-positions of 1,10-phenanthroline)

IT Hydrogenation
(of 3- or 3,8-ethynyl-substituted 1,10-phenanthroline ligands to give ethenyl- and alkyl-substituted derivs.)

IT Dendritic polymers
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of dendrimers contg. ethynyl-linked 3- and 3,8-substituted 1,10-phenanthroline ligands)

IT Polymers, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of polymers contg. ethynyl-linked 3- and 3,8-substituted 1,10-phenanthroline ligands)

IT Bromination
(regioselective; of 1,10-phenanthroline at 3- and 3,8-positions)

IT 536-74-3, Phenylacetylene 705-31-7, 4-Ethynyl(trifluoromethyl)benzene 766-97-2, 4-Ethynyltoluene 768-60-5, 4-Ethynylanisole
RL: RCT (Reactant)
(cross-coupling reaction with 3,8-dibromo-1,10-phenanthroline ligand)

IT 935-14-8, 1,4-Diethynylbenzene 38215-38-2, 4,4'-Diethynyl-1,1'-biphenyl
RL: RCT (Reactant)
(cross-coupling with ruthenium complex of 3-bromo-1,10-phenanthroline)

IT 624-38-4, 1,4-Diiodobenzene 3001-15-8, 4,4'-Diiodobiphenyl
RL: RCT (Reactant)
(cross-coupling with ruthenium complex of 3-ethynyl-1,10-phenanthroline)

IT 38386-99-1, Dipotassium pentachlororuthenate(2-)
RL: RCT (Reactant)
(for prepn. of ruthenium complexes of 1,10-phenanthroline substituted with phenylethynyl groups at 3- or 3,8-positions)

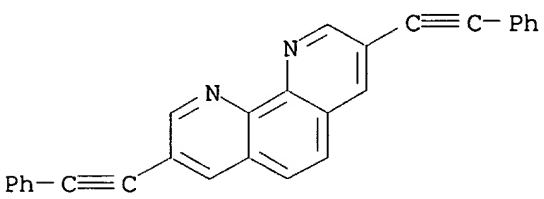
IT 7726-95-6, Bromine, reactions
RL: RCT (Reactant)
(for regioselective bromination of 1,10-phenanthroline)

IT 66127-01-3P, 3-Bromo-1,10-phenanthroline 100125-12-0P, 3,8-Dibromo-1,10-phenanthroline
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Pd-mediated cross-coupling with phenylacetylenes)

IT **168003-69-8P 168003-70-1P 168003-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with ruthenium)

IT 178314-95-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cross-coupling with diiodobenzene or diiodobiphenyl)

IT 178314-93-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cross-coupling with phenylacetylene and analogs)
IT **168003-72-3P 168003-74-5P 168003-76-7P**
168003-78-9P 178314-97-1P 178314-99-3P
178315-01-0P 178315-03-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 66-71-7DP, 1,10-Phenanthroline, acetylenic derivs.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of phenylethynyl 1,10-phenanthroline ligands substituted in 3- or 3,8-positions and complexation with ruthenium)
IT 18851-33-7, 1,10-Phenanthroline monohydrochloride monohydrate
RL: RCT (Reactant)
(regioselective bromination in 3- and 3,8-positions)
IT 98-95-3, Nitrobenzene, uses 108-86-1, Bromobenzene, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(solvent for regioselective bromination of 1,10-phenanthroline in 3- and 3,8-positions)
IT **168003-69-8P 168003-70-1P 168003-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with ruthenium)
RN 168003-69-8 HCAPLUS
CN 1,10-Phenanthroline, 3,8-bis(phenylethynyl)- (9CI) (CA INDEX NAME)



RN 168003-70-1 HCAPLUS
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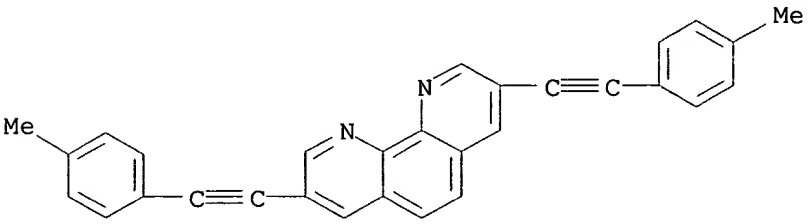
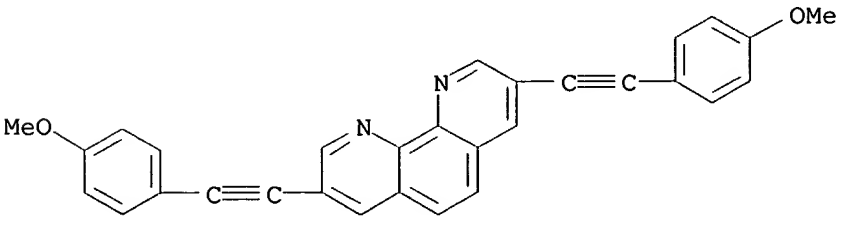
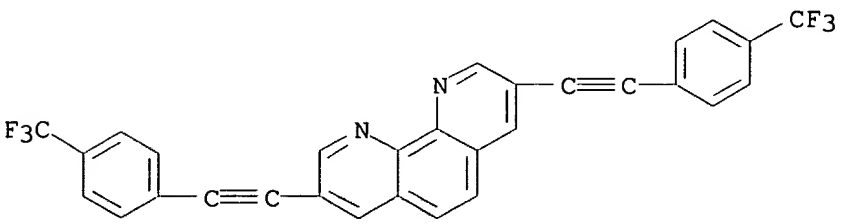


RN 168003-71-2 HCAPLUS
CN 1,10-Phenanthroline, 3,8-bis[(4-methoxyphenyl)ethynyl]- (9CI) (CA INDEX NAME)



IT **168003-72-3P 168003-74-5P 168003-76-7P**
168003-78-9P 178314-97-1P 178314-99-3P
178315-01-0P 178315-03-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 168003-72-3 HCAPLUS
CN 1,10-Phenanthroline, 3,8-bis[[4-(trifluoromethyl)phenyl]ethynyl]-
(9CI) (CA INDEX NAME)



RN 168003-74-5 HCAPLUS
CN Ruthenium(2+), tris[3,8-bis(phenylethynyl)-1,10-phenanthroline-
.kappa.N1,.kappa.N10]-, (OC-6-11)-, bis[hexafluorophosphate(1-)]
(9CI) (CA INDEX NAME)

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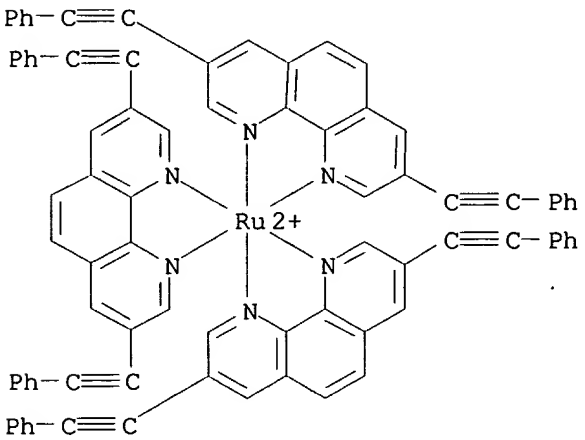
CRN 168003-73-4
CMF C84 H48 N6 Ru
CCI CCS
CDES 7:OC-6-11



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CRN 16919-18-9
CMF F6 P
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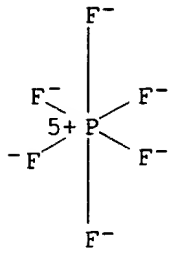

RN 168003-76-7 HCAPLUS
CN Ruthenium(2+), tris[3,8-bis[(4-methylphenyl)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-11)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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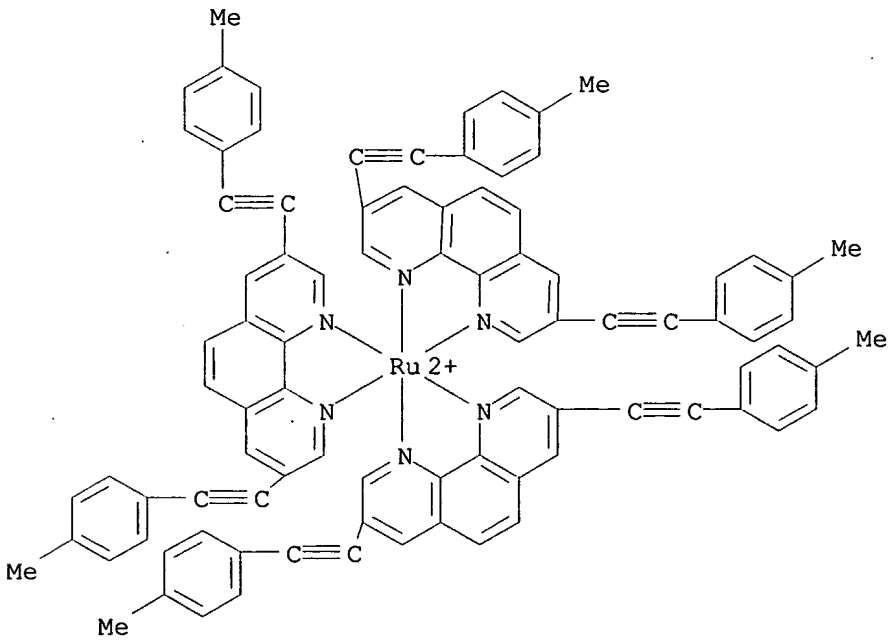
CDES 7:OC-6-11



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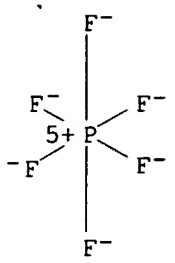
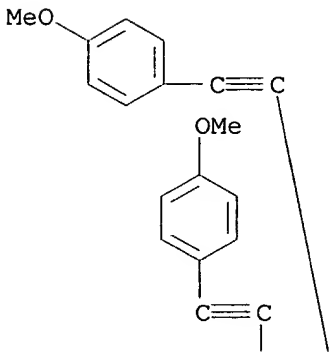


RN 168003-78-9 HCAPLUS
CN Ruthenium(2+), tris[3,8-bis[(4-methoxyphenyl)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-11)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 168003-77-8
CMF C90 H60 N6 O6 Ru
CCI CCS
CDES 7:OC-6-11

PAGE 1-A



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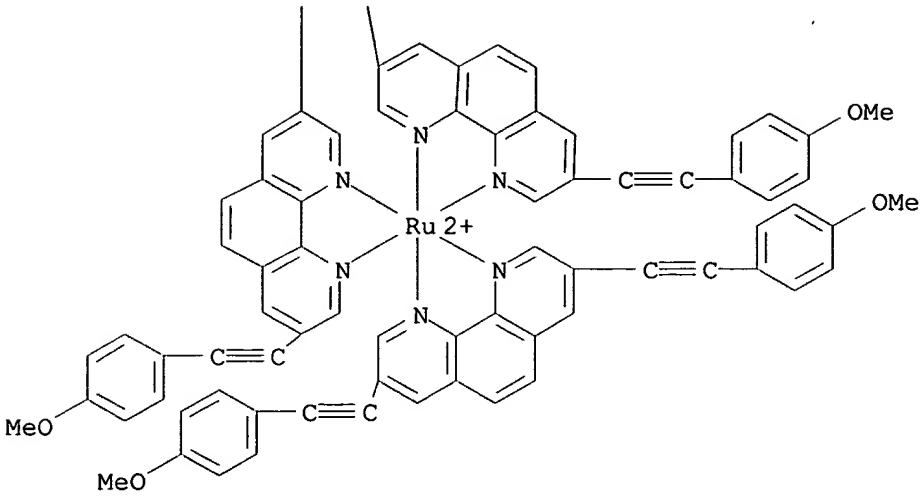

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CRN 16919-18-9
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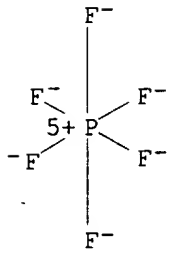

RN 178314-97-1 HCAPLUS
CN Ruthenium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[3-[(4-methylphenyl)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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CRN 178314-96-0
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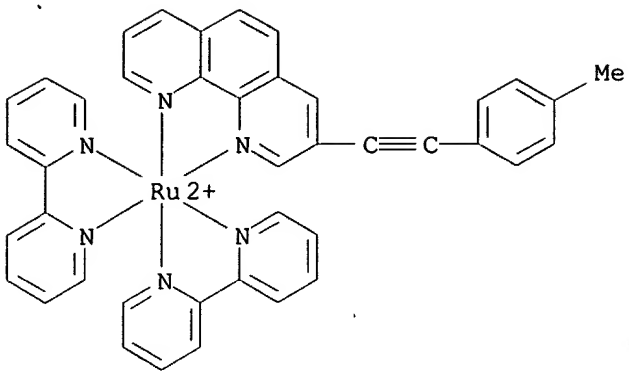
CDES 7:OC-6-33



CM 2

CRN 16919-18-9
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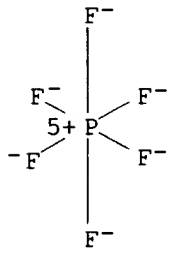

RN 178314-99-3 HCAPLUS
CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,4-phenylenedi-2;1-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

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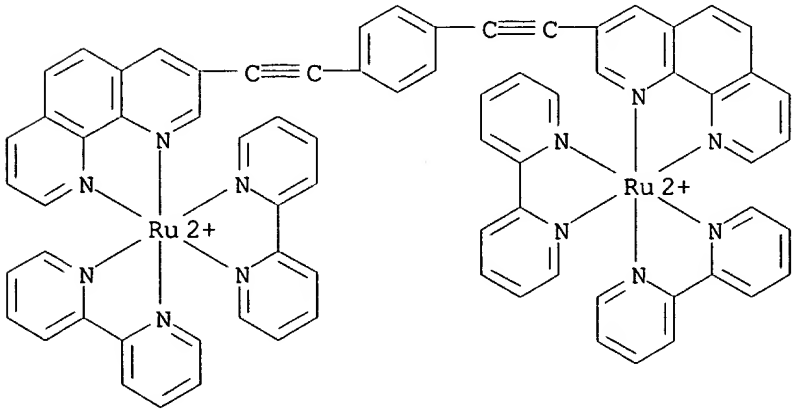

CM 2

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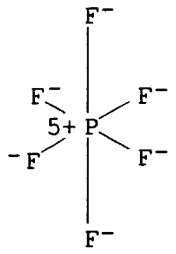
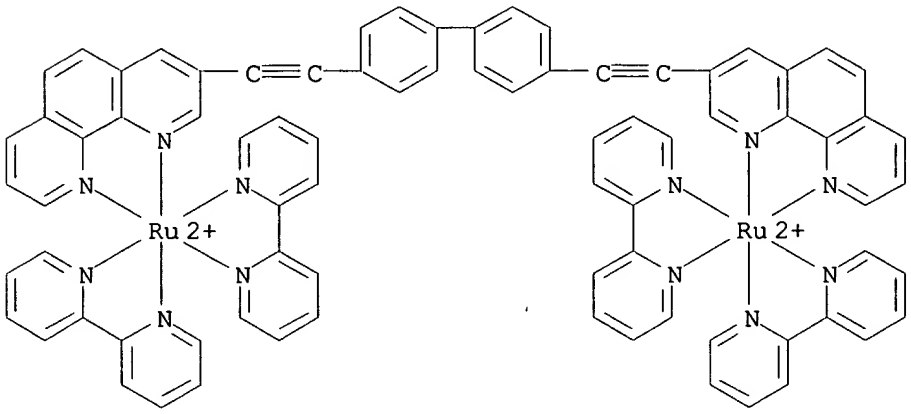


RN 178315-01-0 HCAPLUS
CN Ruthenium(4+), [.mu.-[3,3'-([1,1'-biphenyl]-4,4'-diyldi-2,1-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

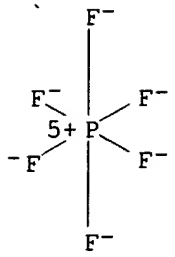
CM 1

CRN 178315-00-9
CMF C80 H54 N12 Ru2
CCI CCS



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

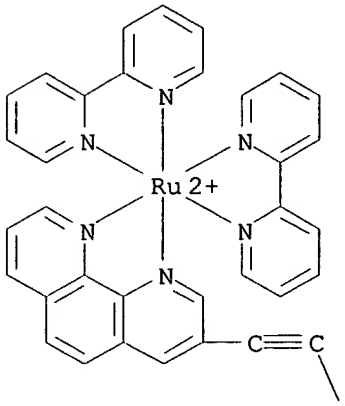


RN 178315-03-2 HCAPLUS
CN Ruthenium(6+), [.mu.3-[3,3',3''-(1,3,5-benzenetriyltri-2,1-ethynediyl)tris[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]hexakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')tri-, hexakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 178315-02-1
CMF C108 H72 N18 Ru3
CCI CCS

PAGE 1-A



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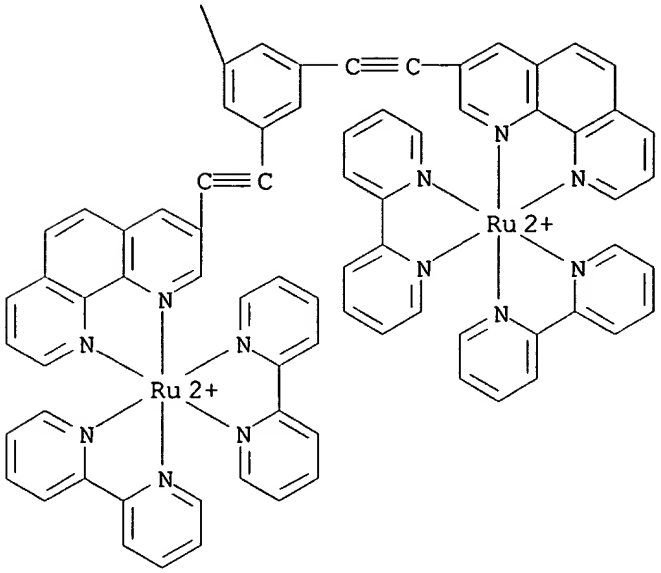
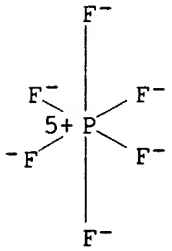


CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1997:582230 Document No. 127:228809 Metal ion complexation induces the assembly of hyperbranched structures. Tzalis, Dimitrios; Glazer, Edith C.; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California, La Jolla, CA, 92093-0358, USA). Polym. Mater. Sci. Eng., 77, 216-217 (English) 1997. CODEN: PMSEDG. ISSN: 0743-0515. Publisher: American Chemical Society.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The phenanthrolinic dendron (I) was prepd. and reacted with [Cu(CH3CN)4]PF6 in CH3CN to yield [Cu(I)2]PF6 in 81 % yield. Reacting I with FeSO4.cntdot.7 H2O in methanolic soln. yielded octahedral [Fe(I)3](PF6)2, an assembly contg. 18 hydroxyl groups that surround an octahedral Fe+2 center. The hexaallyl ligand (II)

was also prepd. and treated with [Cu(CH3CN)4]PF6 in CH3CN to give tetrahedral [Cu(II)2]PF6 in 53% yield. Complexation of II with K2RuCl5 in DMF in the presence of the reducing agent (NaH2PO2), followed by the addn. of excess KPF6, afforded [Ru(II)3](PF6)2, an assembly contg. 18 allyl groups that surround an octahedral center. The results demonstrate that hyperbranched structures can be assembled around metal ions as the structural core instead of a polyfunctional core.

CC 78-7 (Inorganic Chemicals and Reactions)

ST hydroxypropyloxymethylethyloxymethylphenylethynylphenanthroline dendron prepn copper iron complex; allyloxymethylethyloxymethylpheny lethynylphenanthroline dendron prepn copper ruthenium complex; copper hyperbranched phenanthrolinic dendron complex prepn; iron hyperbranched phenanthrolinic dendron complex prepn; ruthenium hyperbranched phenanthrolinic dendron complex prepn; transition metal phenanthrolinic dendron complex prepn

IT Transition metal complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(with self-assembled dendritic-like structures)

IT 115-19-5, 2-Methyl-3-butyn-2-ol 589-15-1, 4-Bromobenzyl bromide 1066-54-2, Trimethylsilylacetylene 1471-17-6, Pentaerythritol triallyl ether 38386-99-1, Dipotassium pentachlororuthenate(2-) 100125-12-0, 3,8-Dibromo-1,10-phenanthroline
RL: RCT (Reactant)
(for prepn. of dendritic structures assembled around transition metal ions)

IT 184102-93-0P 184102-94-1P 184102-95-2P 184102-96-3P **184102-97-4P** 194662-83-4P 194662-84-5P **194662-85-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of dendritic structures assembled around transition metal ions)

IT 64443-05-6, Tetrakis(acetonitrile)copper(1+) hexafluorophosphate
RL: RCT (Reactant)
(prepn. of)

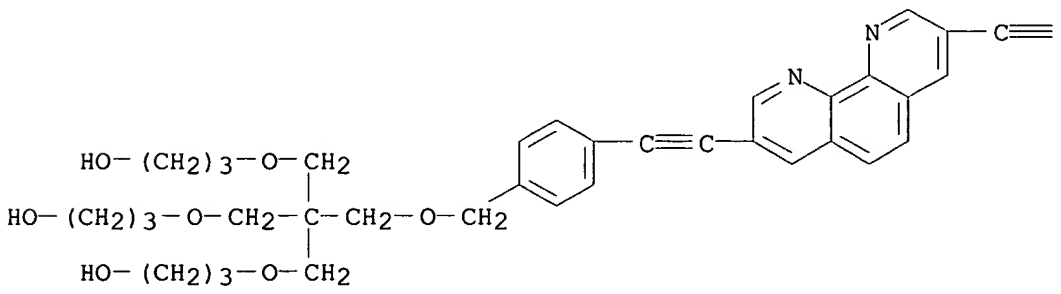
IT **184102-99-6P 184103-01-3P 194662-87-8P 194662-89-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **184102-97-4P 194662-85-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of dendritic structures assembled around transition metal ions)

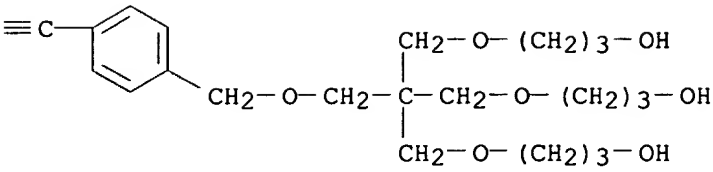
RN 184102-97-4 HCAPLUS

CN 1-Propanol, 3,3'-[[2-[[[4-[[8-[[4-[[3-(3-hydroxypropoxy)-2,2-bis[(3-hydroxypropoxy)methyl]propoxy]methyl]phenyl]ethynyl]-1,10-phenanthrolin-3-yl]ethynyl]phenyl]methoxy]methyl]-2-[(3-hydroxypropoxy)methyl]-1,3-propanediyl]bis(oxy)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

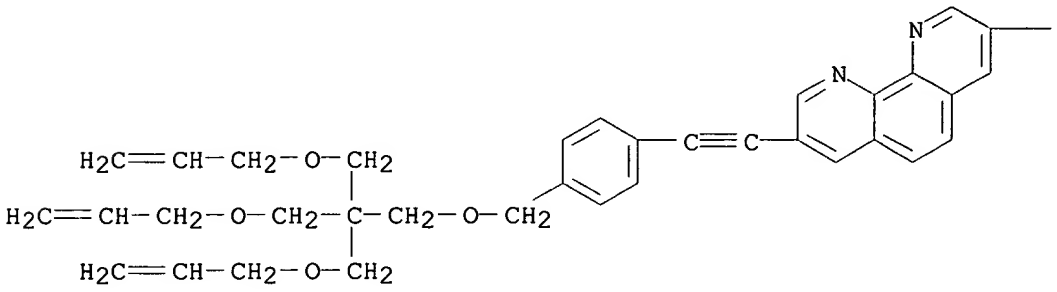


PAGE 1-B



RN 194662-85-6 HCAPLUS
CN 1,10-Phenanthroline, 3,8-bis[[4-[[3-(2-propenyloxy)-2,2-bis[(2-propenyloxy)methyl]propoxy]methyl]phenyl]ethynyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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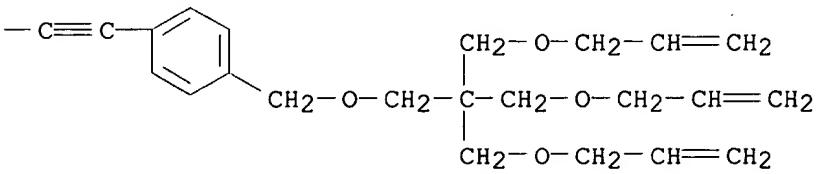
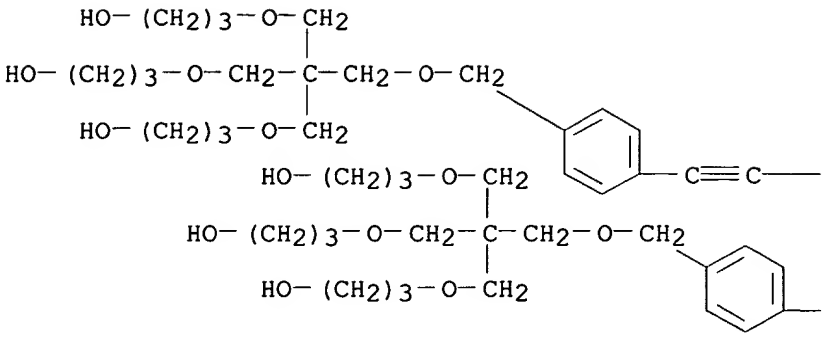


IT **184102-99-6P 184103-01-3P 194662-87-8P 194662-89-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 184102-99-6 HCAPLUS
CN Copper(1+), bis[3,3'-[(1,10-phenanthroline-3,8-diyl-.kappa.N1,.kappa.N10)bis[2,1-ethynediyl-4,1-phenylenemethyleneoxy[2,2-bis[(3-hydroxypropoxy)methyl]-3,1-propanediyl]oxy]]bis[1-propanol]]-, (T-4)-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)

CM 1

CRN 184102-98-5
CMF C116 H152 Cu N4 O28
CCI CCS
CDES 7:T-4

PAGE 1-A



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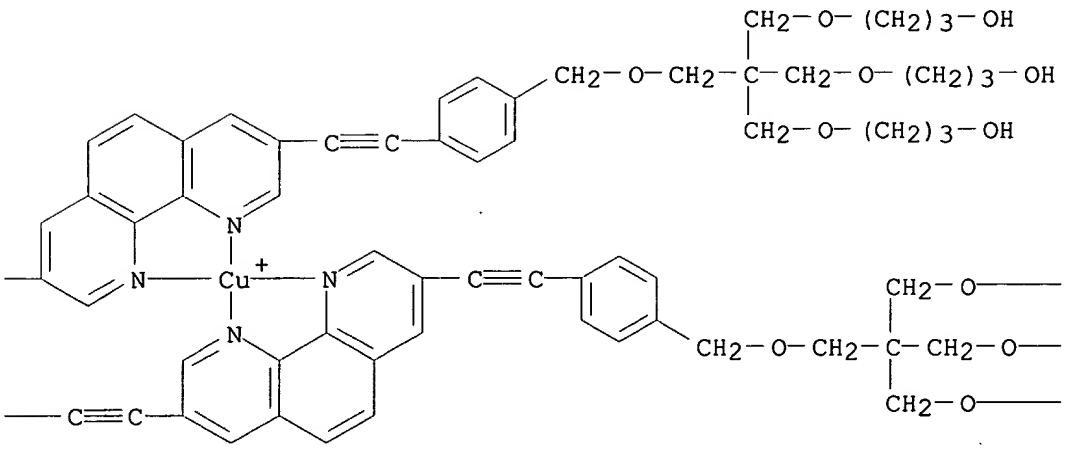


PAGE 1-C

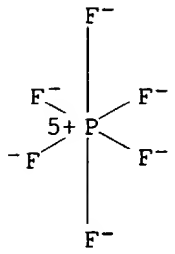
— $(CH_2)_3$—OH

—— $(CH_2)_3$—OH

— $(CH_2)_3$—OH

CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

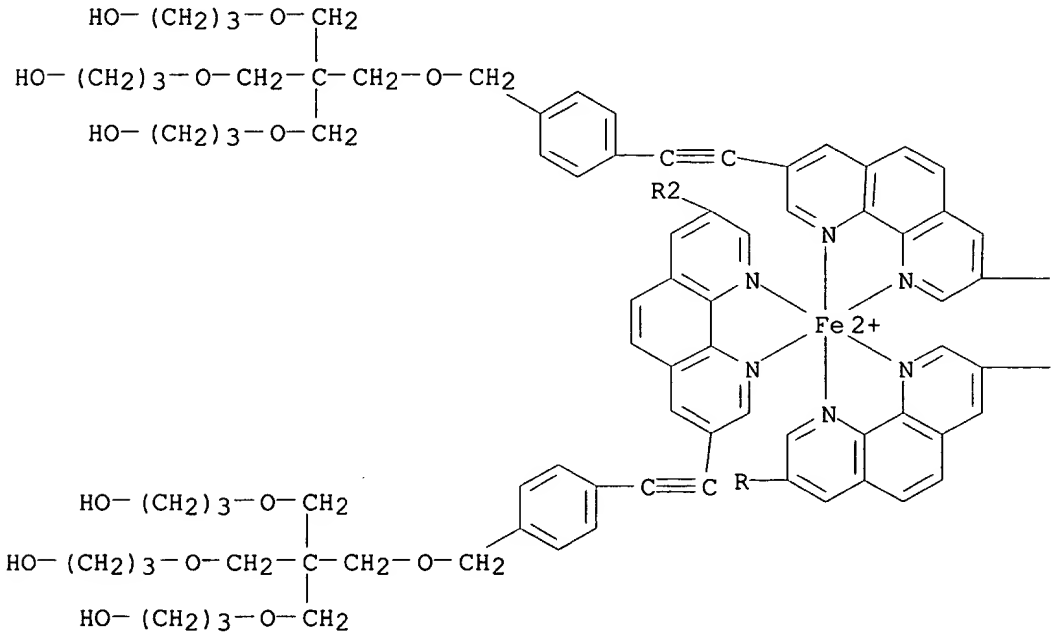


RN 184103-01-3 HCAPLUS
CN Iron(2+), tris[3,3'-[(1,10-phenanthroline-3,8-diyl-.kappa.N1,.kappa.N10)bis[2,1-ethynediyl-4,1-phenylenemethyleneoxy[2,2-bis[(3-hydroxypropoxy)methyl]-3,1-propanediyl]oxy]]bis[1-propanol]]-, (OC-6-11)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

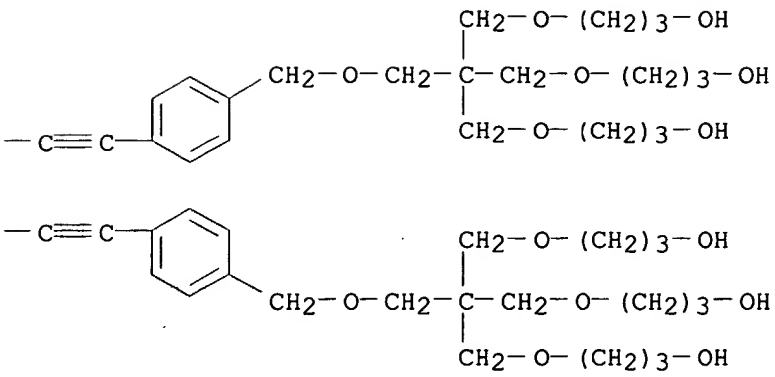
CM 1

CRN 184103-00-2
CMF C174 H228 Fe N6 O42
CCI CCS
CDES 7:OC-6-11

PAGE 1-A



PAGE 1-B



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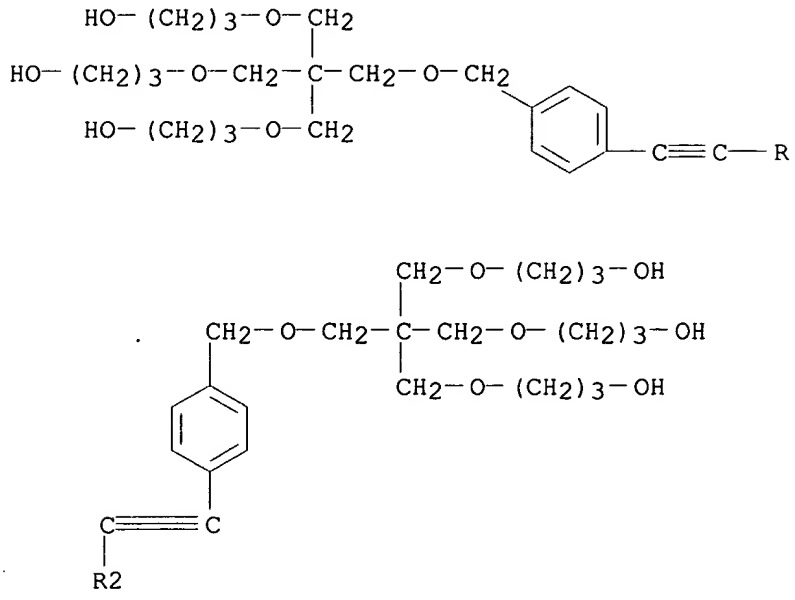
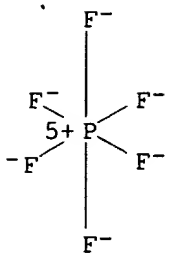


CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

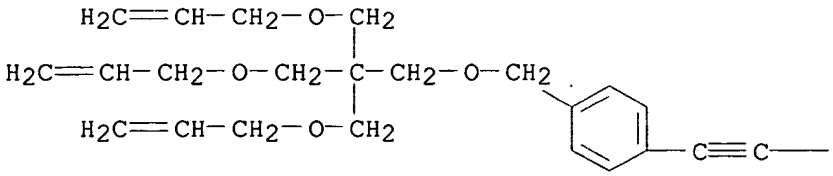


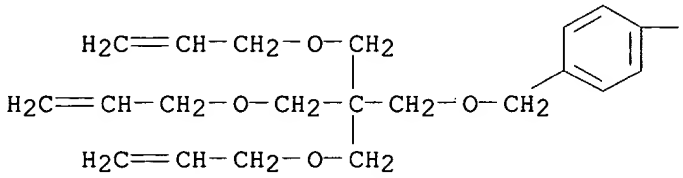
RN 194662-87-8 HCAPLUS
CN Copper(1+), bis[3,8-bis[[4-[[3-(2-propenyloxy)-2,2-bis[(2-propenyloxy)methyl]propoxy]methyl]phenyl]ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (T-4)-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)

CM 1

CRN 194662-86-7
CMF C116 H128 Cu N4 O16
CCI CCS
CDES 7:T-4

PAGE 1-A





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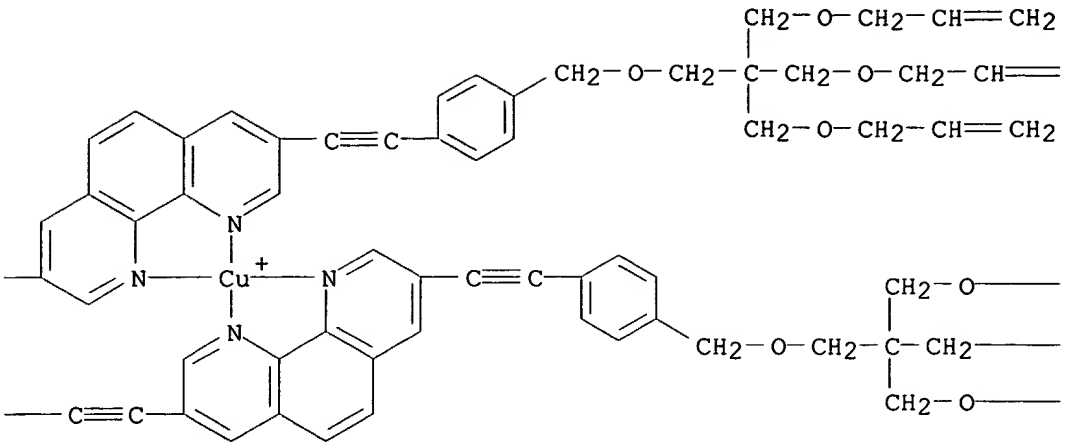

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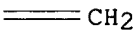
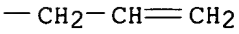
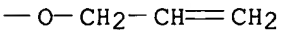
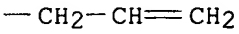


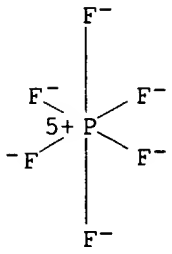






CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



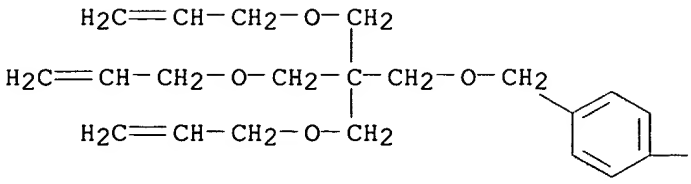
RN 194662-89-0 HCAPLUS
CN Ruthenium(2+), tris[3,8-bis[[4-[[3-(2-propenyloxy)-2,2-bis[(2-propenyloxy)methyl]propoxy]methyl]phenyl]ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-11)-,

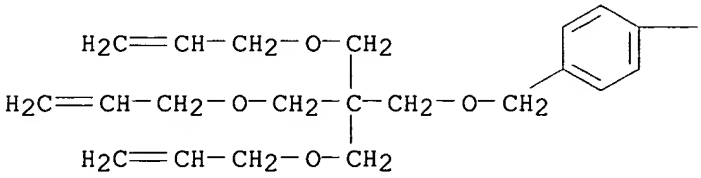
bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 194662-88-9
CMF C174 H192 N6 O24 Ru
CCI CCS
CDES 7:OC-6-11

PAGE 1-A





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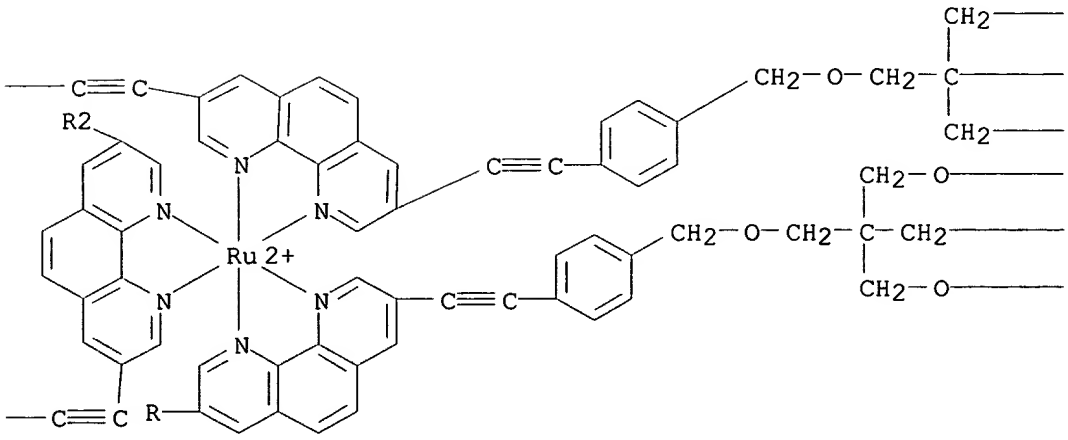

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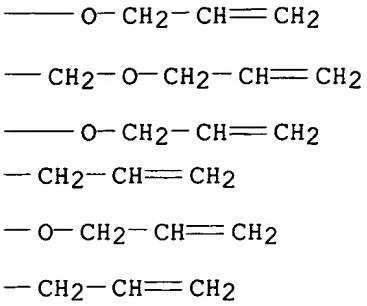

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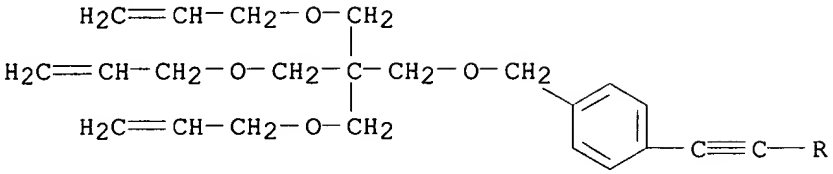
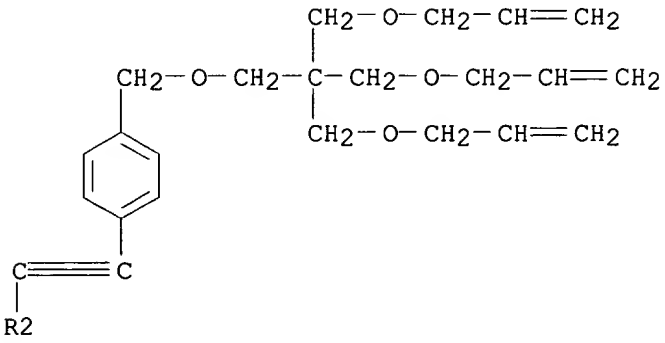
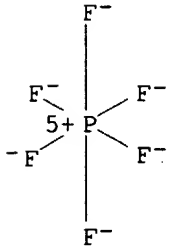




CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1997:21307 Document No. 126:126095 Stereochemically-Defined Supramolecular Architectures: Diastereomerically-Pure Multi-RuII Complexes. Tzalis, Dimitrios; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, CA, 92093-0358, USA). J. Am. Chem. Soc., 119(4), 852-853 (English) 1997. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CJACS-IMAGE; CJACS. Publisher: American Chemical Society.

AB A versatile and efficient approach for the synthesis of diastereomerically-pure multi-RuII arrays is described. Pd-mediated cross-coupling reactions between enantiomerically-pure bromo- and ethynyl-functionalized octahedral RuII complexes afford diastereomerically-pure di- or trinuclear complexes in one step. This simple and modular methodol. opens new routes for the fabrication of multimetallic supramol. assemblies with unique architectures and predetd. abs. configurations at the metal centers.

CC 78-7 (Inorganic Chemicals and Reactions)

ST ruthenium bipyridyl phenanthroline multinuclear diastereomer prepn; cross coupling enantiopure ruthenium octahedral complex

IT Absolute configuration
Diastereomers
(prepn. of diastereomerically-pure multi-Ru(II) complexes with predetd. abs. configuration)

IT Stereochemistry
(stereochem. defined supramol. architecture in prepn. of diastereomerically-pure multi-Ru(II) complexes)

IT Cross-coupling reaction
(stereoselective; of enantiopure bromo- and ethynylphenanthroline ruthenium bipyridine complexes to give diastereomerically-pure multi-Ru(II) complexes)

IT 1066-54-2, Trimethylsilylacetylene 15746-57-3, Bis(2,2'-bipyridine)dichlororuthenium 66127-01-3, 3-Bromo-1,10-phenanthroline 100125-12-0, 3,8-Dibromo-1,10-phenanthroline 123781-93-1, Disodium (-)-O,O'-dibenzoyl-L-tartrate 161374-18-1, Disodium-O,O'-dibenzoyl-D-tartrate
RL: RCT (Reactant)
(prepn. and cross-coupling of enantiopure octahedral ruthenium complexes to give diastereomerically-pure multi-Ru(II) complexes)

IT 161443-93-2P 186179-84-0P 186179-86-2P 186270-08-6P 186270-10-0P 186270-12-2P 186270-14-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cross-coupling of enantiopure octahedral ruthenium complexes to give diastereomerically-pure multi-Ru(II) complexes)

IT **186179-81-7P 186179-88-4P 186270-16-6P 186270-18-8P 186270-22-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cross-coupling of enantiopure octahedral ruthenium complexes to give diastereomerically-pure multi-Ru(II) complexes)

IT 66540-73-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(racemic; prepn. and cross-coupling of enantiopure octahedral ruthenium complexes to give diastereomerically-pure multi-Ru(II) complexes)

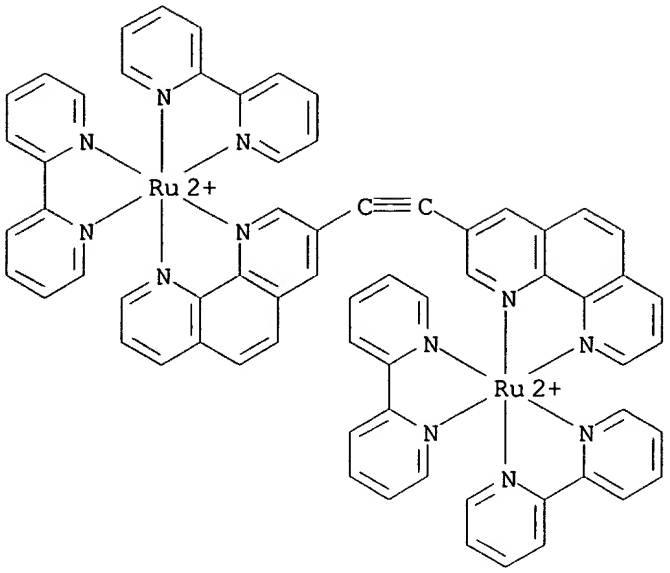
IT **186179-81-7P 186179-88-4P 186270-16-6P 186270-18-8P 186270-22-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cross-coupling of enantiopure octahedral ruthenium complexes to give diastereomerically-pure multi-Ru(II) complexes)

RN 186179-81-7 HCAPLUS

CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, stereoisomer, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

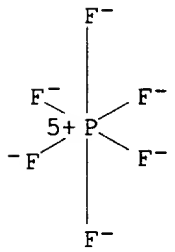
CM 1

CRN 186179-80-6
CMF C66 H46 N12 Ru2
CCI CCS
CDES *



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

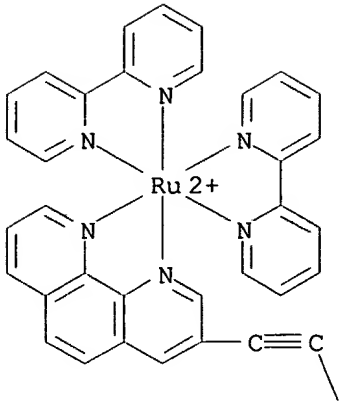


RN 186179-88-4 HCAPLUS
CN Ruthenium(6+), hexakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.3-[3,8-bis[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]]tri-, stereoisomer, hexakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

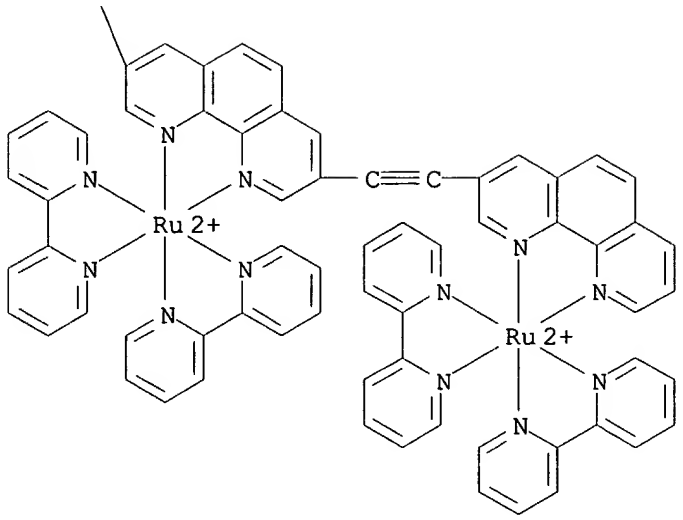
CM 1

CRN 186179-87-3
CMF C100 H68 N18 Ru3
CCI CCS
CDES *

PAGE 1-A

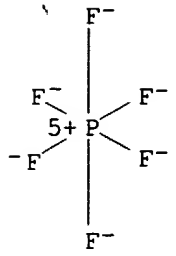


PAGE 2-A



CM 2

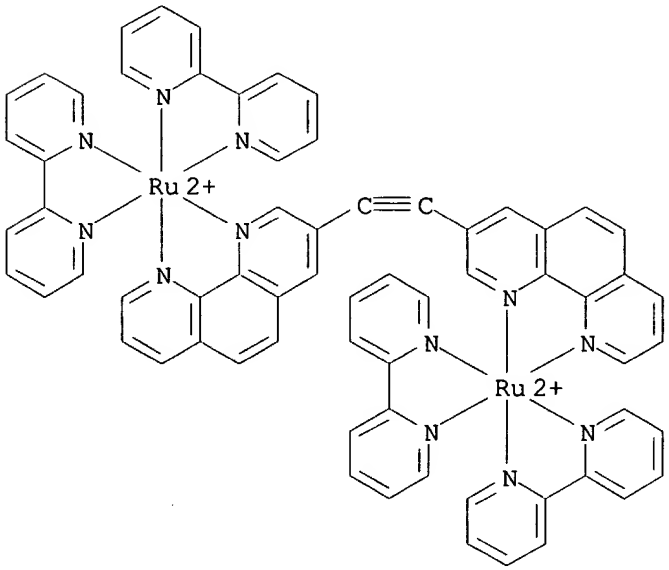
CRN 16919-18-9
CMF F6 P
CCI CCS



RN 186270-16-6 HCAPLUS
CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, stereoisomer, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

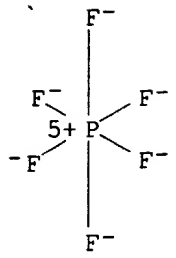
CM 1

CRN 186270-15-5
CMF C66 H46 N12 Ru2
CCI CCS
CDES *



CM 2

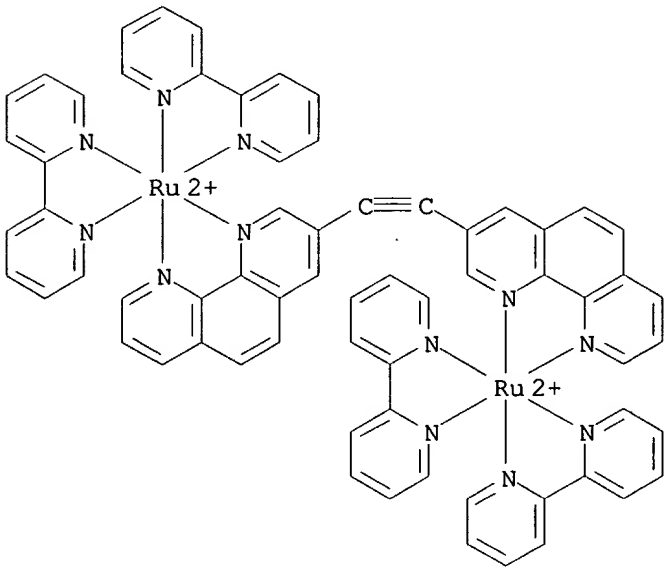
CRN 16919-18-9
CMF F6 P
CCI CCS



RN 186270-18-8 HCAPLUS
CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,2-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, stereoisomer, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

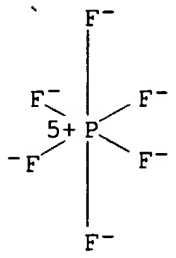
CM 1

CRN 186270-17-7
CMF C66 H46 N12 Ru2
CCI CCS
CDES *



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

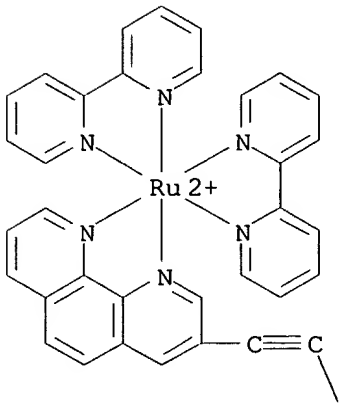


RN 186270-22-4 HCAPLUS
CN Ruthenium(6+), hexakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.3-[3,8-bis[(1,10-phenanthrolin-3-yl-.kappa.N1,.kappa.N10)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]]tri-, stereoisomer, hexakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

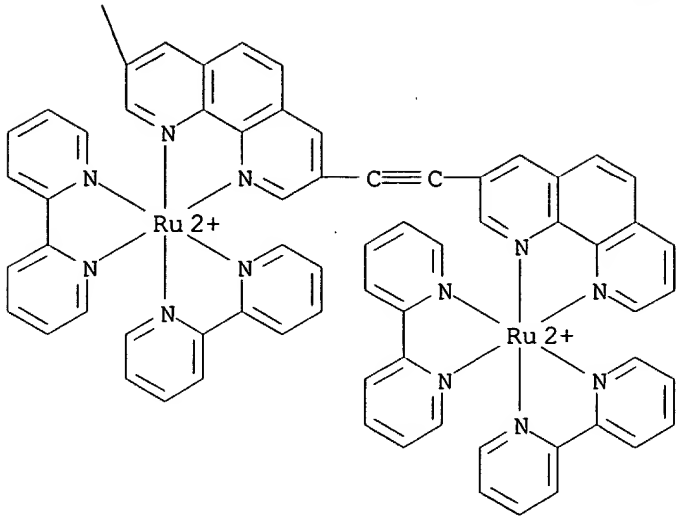
CM 1

CRN 186270-21-3
CMF C100 H68 N18 Ru3
CCI CCS
CDES *

PAGE 1-A

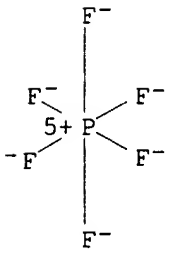


PAGE 2-A



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1996:711178 Document No. 126:25985 Toward self-assembling dendrimers: metal complexation induces the assembly of hyperbranched structures. Tzalis, Dimitrios; Tor, Yitzhak (Dep. Chem. Biochem., Univ. California, San Diego, La Jolla, CA, 92093-0358, USA). Tetrahedron Lett., 37(46), 8293-8296 (English) 1996. CODEN: TELEAY. ISSN: 0040-4039. Publisher: Elsevier.

AB A novel 1,10-phenanthroline ligand, sym. substituted at the 3,8-positions with branched multifunctional groups, is self-assembled into dendritic structures upon metal complexation.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 28

ST transition metal multifunctional phenanthroline dendrimer prepn; copper multifunctional phenanthroline dendrimer prepn; iron multifunctional phenanthroline dendrimer prepn

IT Transition metal compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(phenanthroline complexes; prepn. of copper and iron hyperbranched multifunctional phenanthroline complexes with dendritic structures)

IT 64443-05-6, Tetrakis(acetonitrile)copper(1+) hexafluorophosphate

RL: RCT (Reactant)
(for self-assembly prepn. of copper complex of branched multifunctionally substituted phenanthroline)

IT 115-19-5, 2-Methyl-3-butyn-2-ol 589-15-1, 4-Bromobenzyl bromide 1471-17-6, Pentaerythritol triallyl ether 100125-12-0, 3,8-Dibromo-1,10-phenanthroline
RL: RCT (Reactant)
(for self-assembly prepn. of transition metal complexes of branched multifunctionally substituted phenanthroline)

IT 184102-93-0P 184102-94-1P 184102-95-2P 184102-96-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for self-assembly prepn. of transition metal complexes of branched multifunctionally substituted phenanthroline)

IT **184102-97-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and self-assembly into dendritic structures upon metal complexation)

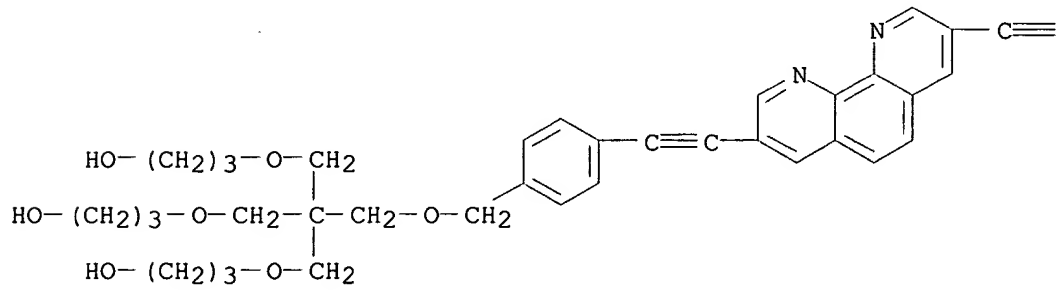
IT **184102-99-6P 184103-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(self-assembly prepn. of dendrimer)

IT **184102-97-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and self-assembly into dendritic structures upon metal complexation)

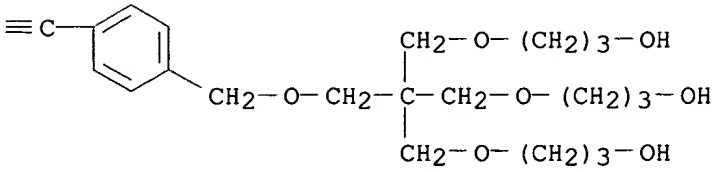
RN 184102-97-4 HCAPLUS

CN 1-Propanol, 3,3'-[[2-[[[4-[[8-[[4-[[3-(3-hydroxypropoxy)-2,2-bis[(3-hydroxypropoxy)methyl]propoxy]methyl]phenyl]ethynyl]-1,10-phenanthrolin-3-yl]ethynyl]phenyl]methoxy]methyl]-2-[(3-hydroxypropoxy)methyl]-1,3-propanediyl]bis(oxy)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT **184102-99-6P 184103-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(self-assembly prepn. of dendrimer)

RN 184102-99-6 HCAPLUS

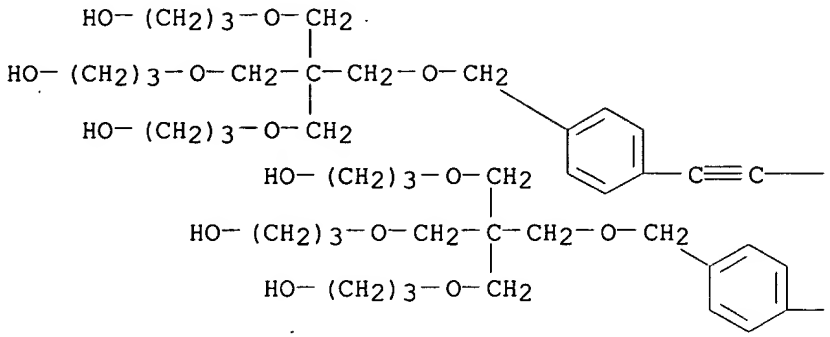
CN Copper(1+), bis[3,3'-[(1,10-phenanthroline-3,8-diyl-.kappa.N1,.kappa.N10)bis[2,1-ethynediyl-4,1-phenylenemethyleneoxy[2,2-bis[(3-hydroxypropoxy)methyl]-3,1-

propanediyl]oxy]]bis[1-propanol]]-, (T-4)-, hexafluorophosphate(1-) (9CI) (CA INDEX NAME)

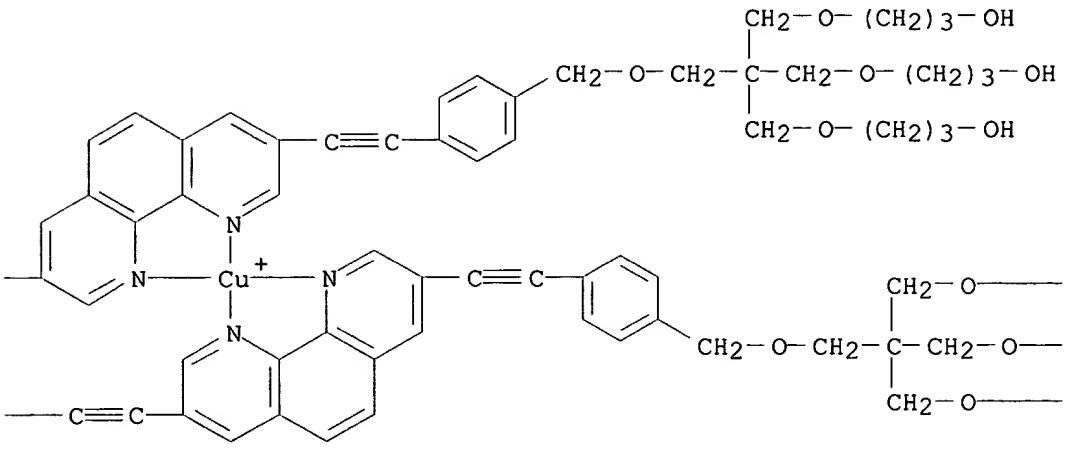
CM 1

CRN 184102-98-5
CMF C116 H152 Cu N4 O28
CCI CCS
CDES 7:T-4

PAGE 1-A



PAGE 1-B



PAGE 1-C

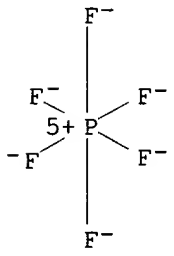
— $(CH_2)_3$ — OH

—— $(CH_2)_3$ — OH

— $(CH_2)_3$ — OH

CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

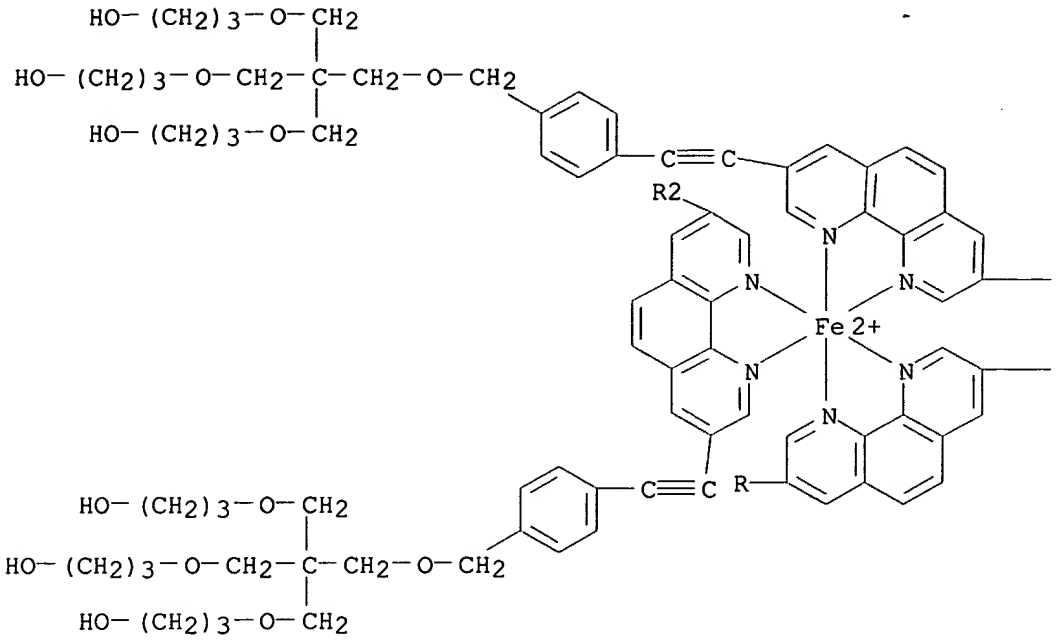


RN 184103-01-3 HCAPLUS
CN Iron(2+), tris[3,3'-[(1,10-phenanthroline-3,8-diyl-.kappa.N1,.kappa.N10)bis[2,1-ethynediyl-4,1-phenylenemethyleneoxy[2,2-bis[(3-hydroxypropoxy)methyl]-3,1-propanediyl]oxy]]bis[1-propanol]]-, (OC-6-11)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

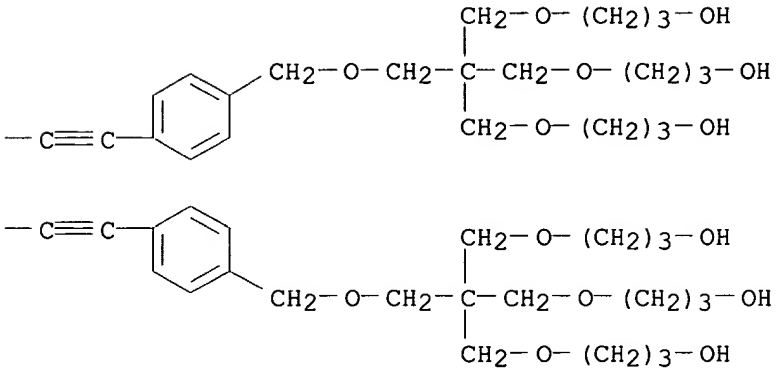
CM 1

CRN 184103-00-2
CMF C174 H228 Fe N6 O42
CCI CCS
CDES 7:OC-6-11

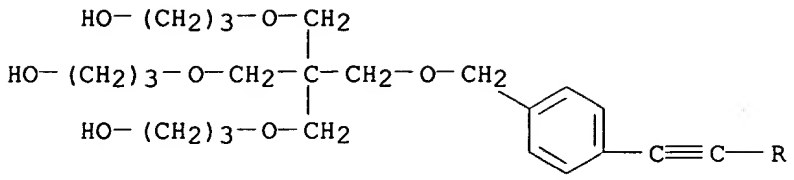
PAGE 1-A

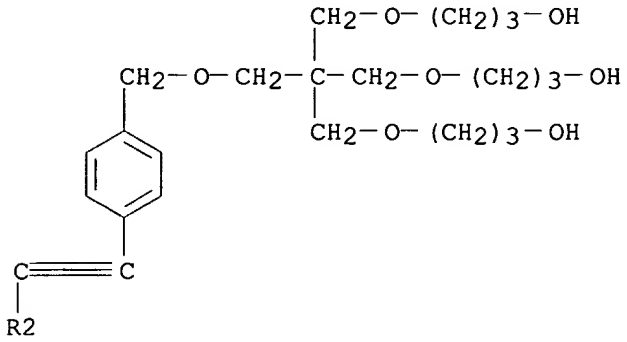


PAGE 1-B



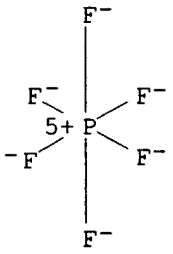
PAGE 2-A





CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1996:311921 Document No. 125:74618 Coordination compounds as building blocks: single-step synthesis of multi-ruthenium(II) complexes. Tzalis, Dimitrios; Tor, Yitzhak (Dep. Chemistry, Univ. California, San Diego, La Jolla, CA, 92093-0358, USA). Chem. Commun. (Cambridge) (9), 1043-1044 (English) 1996. CODEN: CHCOFS. ISSN: 1359-7345.
AB Pd-mediated cross-coupling reactions of [(bpy)2Ru(3-bromo-1,10-phenanthroline)](PF6-)2 with various arom. acetylenes and of [(bpy)2Ru(3-ethynyl-1,10-phenanthroline)](PF6-)2 with arom. iodides gave mono-, di- and tri-nuclear complexes in high yields and under mild conditions.
CC 78-7 (Inorganic Chemicals and Reactions)
ST ruthenium multinuclear diimine acetylene coupled prepn
IT 7681-65-4, Cuprous iodide 13965-03-2, Dichlorobis(triphenylphosphine)palladium
RL: CAT (Catalyst use); USES (Uses)

(for prepn. of ruthenium multinuclear bipyridine/phenanthroline deriv. complexes by cross-coupling via arom. acetylenes or iodides)

IT 624-38-4, 1,4-Diiodobenzene 766-97-2, 4-Ethynyltoluene 935-14-8, 1,4-Diethynylbenzene 3001-15-8, 4,4'-Diiodobiphenyl 7567-63-7, 1,3,5-Triethynylbenzene 15746-57-3, Bis(2,2'-bipyridine)dichlororuthenium 38215-38-2, 4,4'-Diethynyl-1,1'-biphenyl 66127-01-3, 3-Bromo-1,10-phenanthroline 178315-04-3, 3-Ethynyl-1,10-phenanthroline
RL: RCT (Reactant)
(for prepn. of ruthenium multinuclear bipyridine/phenanthroline deriv. complexes by cross-coupling via arom. acetylenes or iodides)

IT 178314-93-7P 178314-95-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of ruthenium multinuclear bipyridine/phenanthroline deriv. complexes by cross-coupling via arom. acetylenes or iodides)

IT **178314-97-1P 178314-99-3P 178315-01-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and electronic spectra of)

IT **178315-03-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of ruthenium multinuclear bipyridine phenanthroline deriv. complexes by cross-coupling via arom. acetylenes or iodides)

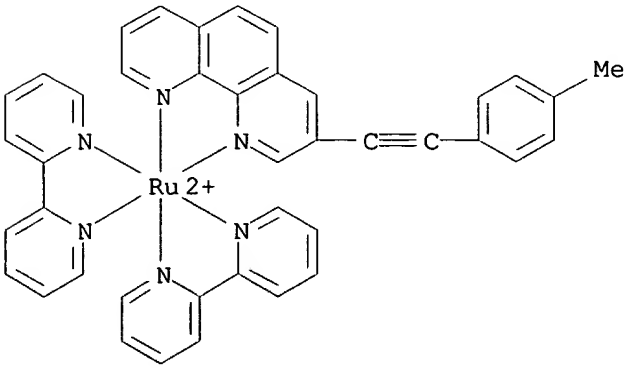
IT **178314-97-1P 178314-99-3P 178315-01-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and electronic spectra of)

RN 178314-97-1 HCAPLUS

CN Ruthenium(2+), bis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[3-[(4-methylphenyl)ethynyl]-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-33)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

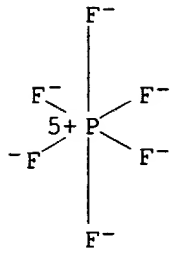
CRN 178314-96-0
CMF C41 H30 N6 Ru
CCI CCS
CDES 7:OC-6-33



CM 2

CRN 16919-18-9
CMF F6 P

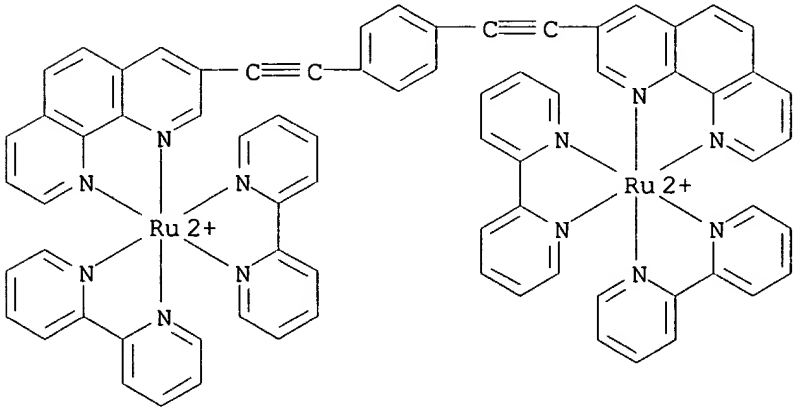
CCI CCS



RN 178314-99-3 HCAPLUS
CN Ruthenium(4+), tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')[.mu.-[3,3'-(1,4-phenylenedi-2,1-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

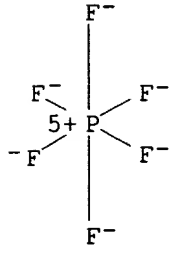
CM 1

CRN 178314-98-2
CMF C74 H50 N12 Ru2
CCI CCS



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS

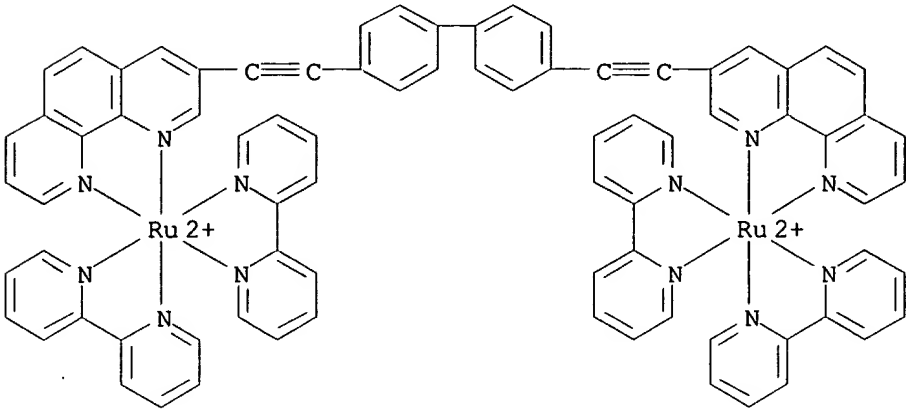


RN 178315-01-0 HCAPLUS

CN Ruthenium(4+), [.mu.-[3,3'-([1,1'-biphenyl]-4,4'-diyldi-2,1-ethynediyl)bis[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]tetrakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')di-, tetrakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

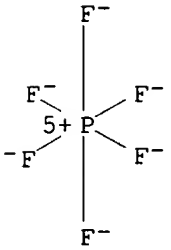
CM 1

CRN 178315-00-9
CMF C80 H54 N12 Ru2
CCI CCS



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



IT **178315-03-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of ruthenium multinuclear bipyridine phenanthroline deriv. complexes by cross-coupling via arom. acetylenes or iodides)

RN 178315-03-2 HCAPLUS
CN Ruthenium(6+), [.mu.3-[3,3',3''-(1,3,5-benzenetriyltri-2,1-ethynediyl)tris[1,10-phenanthroline-.kappa.N1,.kappa.N10]]]hexakis(2,2'-bipyridine-.kappa.N1,.kappa.N1')tri-, hexakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

CM 1

CRN 178315-02-1
CMF C108 H72 N18 Ru3
CCI CCS

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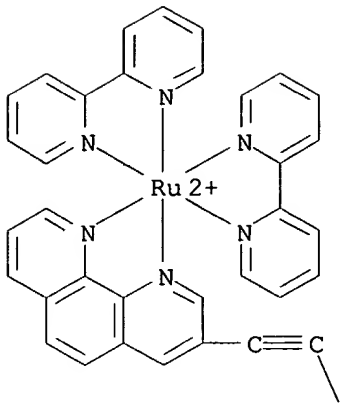
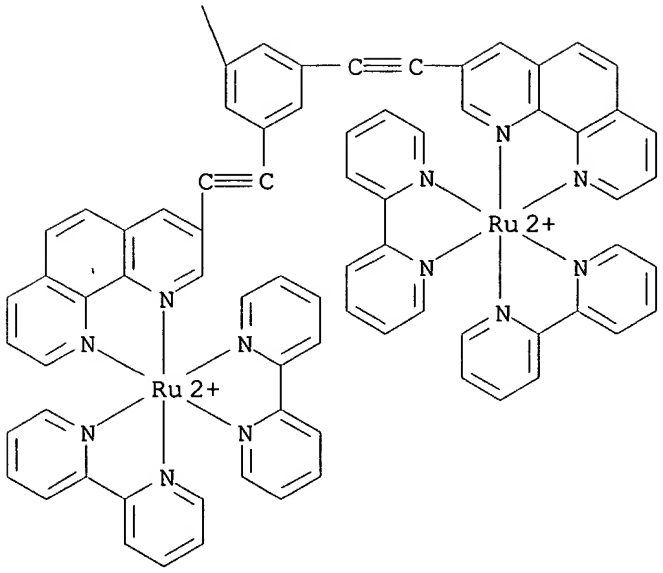
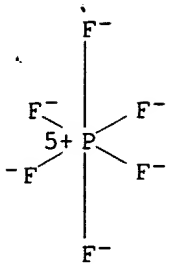


PAGE 2-A



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



L68 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 1998 ACS
1995:771815 Document No. 123:216854 Tuning the electronic properties of phenanthroline ligands: 3,8-bis(arylethynyl)-1,10-phenanthrolines and their Ru(II) complexes. Tzalis, Dimitrios; Tor, Yitzhak (Dep. Chem. Biochem., Univ. California, San Diego, La Jolla, CA, 92093-0358, USA). Tetrahedron Lett., 36(34), 6017-20 (English) 1995. CODEN: TELEAY. ISSN: 0040-4039.

AB Pd-catalyzed cross-coupling reactions between 3,8-dibromo-1,10-phenanthroline and substituted phenylacetylenes provide a novel family of highly conjugated metal chelators. The electronic transitions of the ligands and their Ru(II) complexes are affected by the nature of the substituents on the conjugated Ph rings.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 27, 73

ST ruthenium bisarylethynylphenanthroline prepn substituent electronic tuning; arylethynylphenanthroline ruthenium prepn substituent electronic tuning; phenanthroline bisarylethynyl deriv ruthenium prepn substituent; UV ruthenium bisarylethynylphenanthroline substituent electronic tuning

IT Ultraviolet and visible spectra
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

IT 7681-65-4, Copper iodide (CuI) 13965-03-2, Dichlorobis(triphenylphosphine)palladium
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

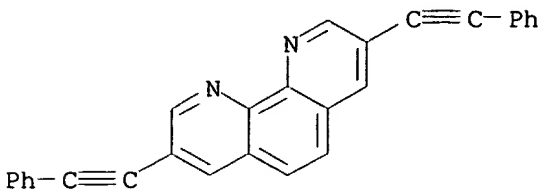
IT **168003-69-8P 168003-70-1P 168003-71-2P 168003-72-3P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

IT **168003-74-5P 168003-76-7P 168003-78-9P 168003-80-3P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

IT 536-74-3 705-31-7, 4-Trifluoromethylphenylacetylene 766-97-2, 4-Methylphenylacetylene 768-60-5, 4-Methoxyphenylacetylene 38386-99-1, Dipotassium pentachlororuthenate(2-) 100125-12-0, 3,8-Dibromo-1,10-phenanthroline
RL: RCT (Reactant)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

IT **168003-69-8P 168003-70-1P 168003-71-2P 168003-72-3P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

RN 168003-69-8 HCAPLUS
CN 1,10-Phenanthroline, 3,8-bis(phenylethynyl)- (9CI) (CA INDEX NAME)



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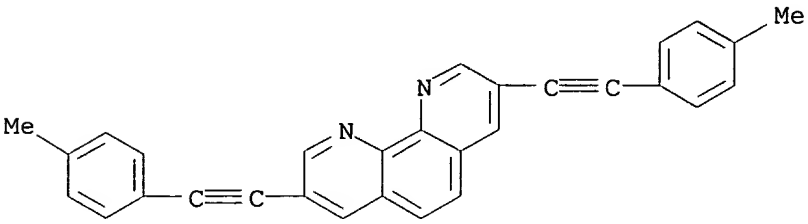

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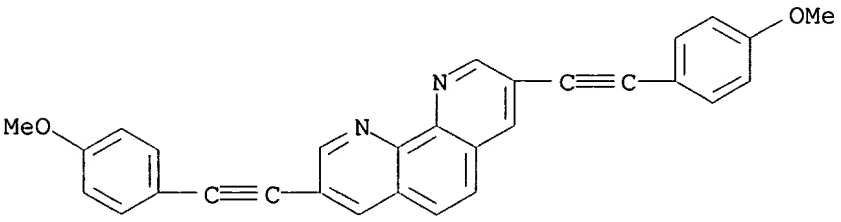

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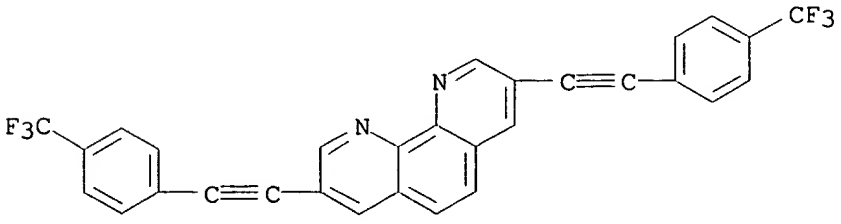

IT **168003-74-5P 168003-76-7P 168003-78-9P 168003-80-3P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tuning of electronic properties of bis(arylethynyl)phenanthrolines and their Ru(II) complexes)

RN 168003-74-5 HCAPLUS
CN Ruthenium(2+), tris[3,8-bis(phenylethynyl)-1,10-phenanthroline-.kappa.N1,.kappa.N10]-, (OC-6-11)-, bis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

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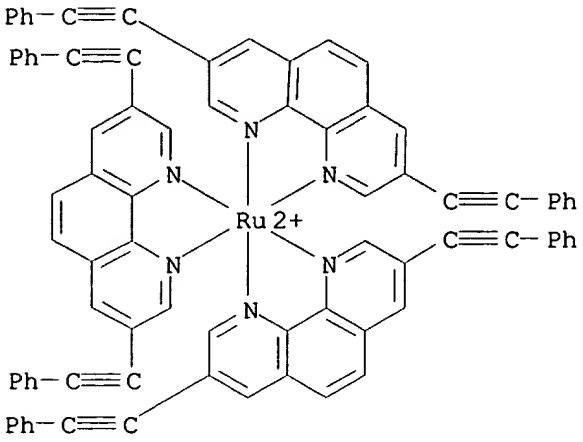
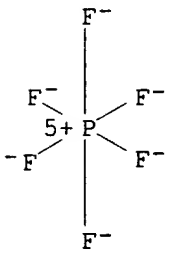
CCI CCS
CDES 7:OC-6-11



CM 2

CRN 16919-18-9
CMF F6 P
CCI CCS



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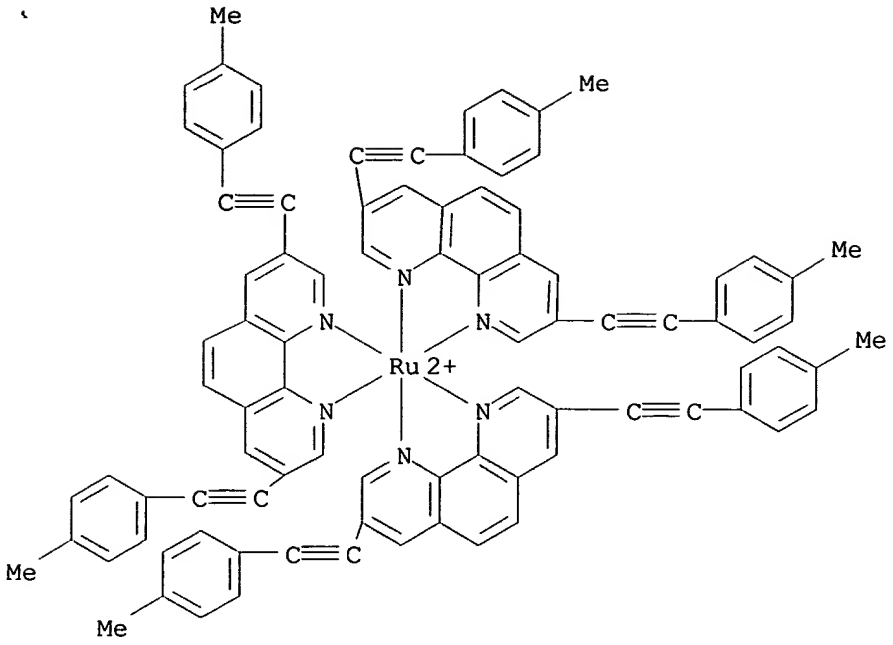
CDES 7:OC-6-11



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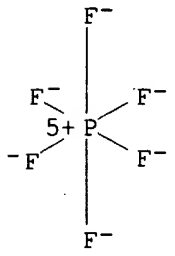

RN 168003-78-9 HCAPLUS
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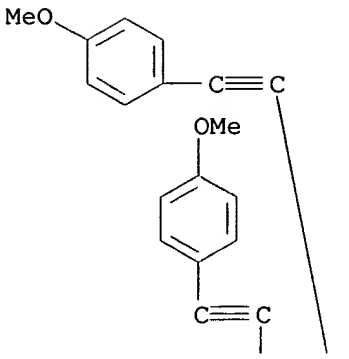
CRN 168003-77-8
CMF C90 H60 N6 O6 Ru
CCI CCS
CDES 7:OC-6-11

PAGE 1-A



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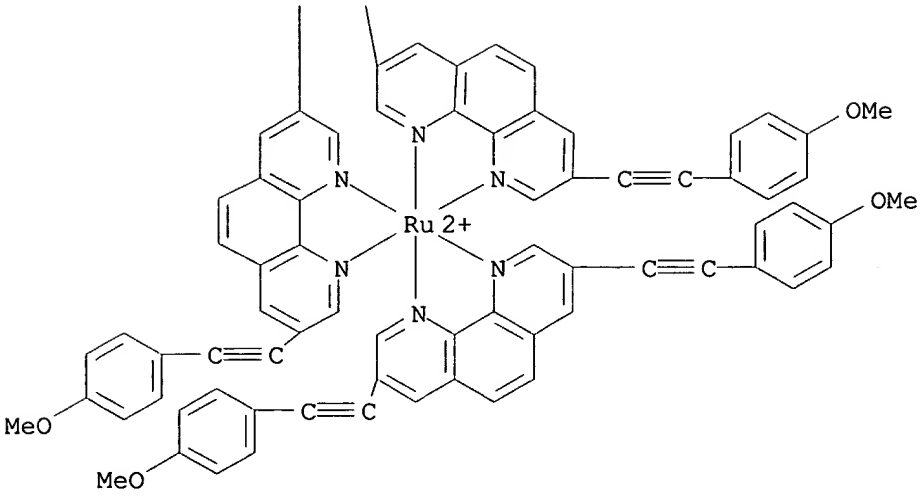

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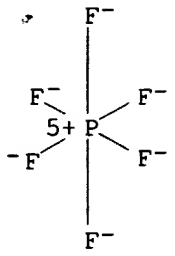

RN 168003-80-3 HCAPLUS
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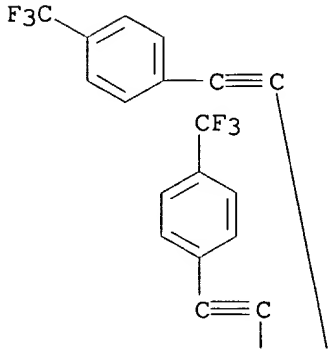
CRN 168003-79-0
CMF C90 H42 F18 N6 Ru
CCI CCS
CDES 7:OC-6-11

PAGE 1-A



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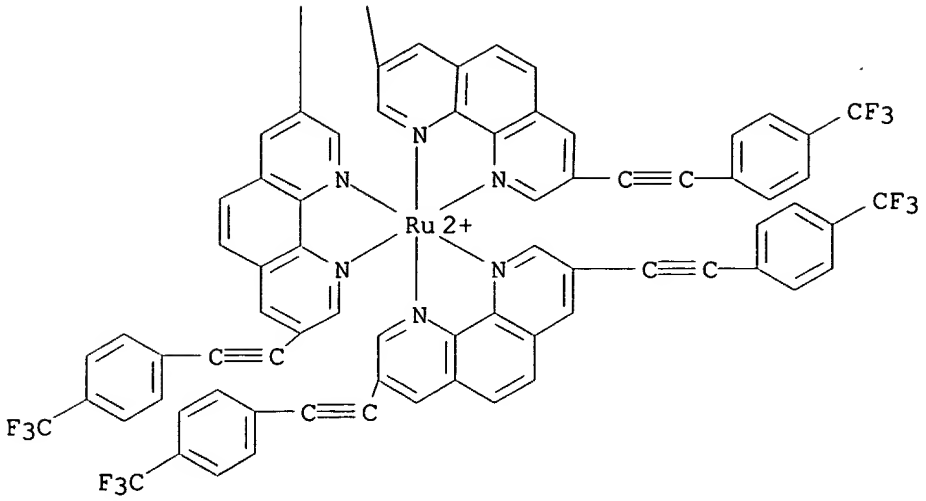

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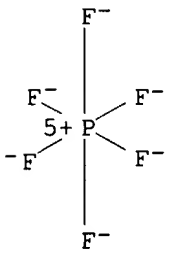

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L72 0 L67

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End of Result Set

L9: Entry 18 of 18 File: USPT Sep 10, 1991

US-PAT-NO: 5047519
DOCUMENT-IDENTIFIER: US 5047519 A
** See image for Certificate of Correction **

TITLE: Alkynylamino-nucleotides

DATE-ISSUED: September 10, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hobbs, Jr.; Frank W.	Wilmington	DE		
Cocuzza; Anthony J.	Wilmington	DE		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
E. I. Du Pont de Nemours and Company	Wilmington	DE			02

APPL-NO: 07/ 057565 [PALM]
DATE FILED: June 12, 1987

PARENT-CASE:
REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of application Ser. No. 881,372, filed July 2, 1986, now abandoned and is related to U.S. Pat. No. 4,833,332 and Method, System and Reagents for DNA Sequencing, Ser. No. 07/057,566, filed concurrently herewith on June 2, 1987, by Prober et al. which is also a continuation-in-part of Ser. No. 881,372.

INT-CL: [05] C07H 1/00

US-CL-ISSUED: 536/23; 536/24, 536/26, 536/27, 536/29, 544/243, 544/244
US-CL-CURRENT: 536/27.14; 514/45, 536/27.2, 544/243, 544/244

FIELD-OF-SEARCH: 536/23, 536/24, 536/28, 536/29, 536/26, 544/244, 544/243

PRIOR-ART-DISCLOSED:

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0251786	January 1988	EP	536/27
0252683	January 1988	EP	536/27
8403285	August 1984	WO	

OTHER PUBLICATIONS

h e b b g e e e f e e e f

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Gibson et al., Nucleic Acids Research; vol. 15; No. 16; 6455-6467 (1987).

ART-UNIT: 183

PRIMARY-EXAMINER: Brown; Johnnie R.

ASSISTANT-EXAMINER: Wilson; James O.

ATTY-AGENT-FIRM: Frank; George A.

ABSTRACT:

Alkynylamino-nucleotides and labeled alkynylamino-nucleotides useful, for example, as chain terminating substrates for DNA sequencing are provided along with several key intermediates and processes for their preparation.

12 Claims, 0 Drawing figures

h e b b g e e e f e e e f

First Hit Fwd Refs

L11: Entry 21 of 28 File: USPT Sep 28, 1999

DOCUMENT-IDENTIFIER: US 5959100 A
TITLE: Pyrimidine nucleosides as therapeutic and diagnostic agents

Abstract Text (1):
Modified nucleosides and methods of making and using the nucleosides are disclosed. The compounds can be prepared by reacting nucleoside starting materials that contain a suitable leaving group at one or more of the carbon atoms in the purine or pyrimidine ring, with a vinylstannane, carbon monoxide, and a palladium catalyst to provide 1-ene-3-one intermediates. These intermediates are then reacted with suitably functionalized primary or secondary amines via a Michael reaction. When the intermediate is a 5-position modified pyrimidine ring, and the amine contains a second hydrogen, it can do a second Michael reaction with the ene-one or the ene-imine in the pyrimidine ring. Appropriate modification of the amine reactant can yield products with various bioactivities. The nucleosides can be used therapeutically as anti-cancer, anti-bacterial or anti-viral drugs. The nucleosides can also be used for diagnostic applications, for example, by incorporating a radiolabel or fluorescent label into the molecule. The nucleosides can be used to prepare oligonucleotides for use in various applications, either alone or in combination with other modified nucleosides and/or naturally occurring nucleosides.

Brief Summary Text (4):
There has been considerable interest in developing modified nucleosides as therapeutic agents, diagnostic agents, and for incorporation into oligonucleotides. For example, modified nucleosides such as AZT, ddI, d4T, and others have been used to treat AIDS. 5-trifluoromethyl-2'-deoxyuridine is active against herpetic keratitis and 5-iodo-1-(2-deoxy-2-fluoro-b-D-arabinofuranosyl)cytosine has activity against CMV, VZV, HSV-1, HSV-2 and EBV (A Textbook of Drug Design and Development, Povl Krogsgaard-Larsen and Hans Bundgaard, Eds., Harwood Academic Publishers, 1991, Ch. 15).

Brief Summary Text (5):
Modified nucleosides have shown utility in diagnostic applications. In these applications, the nucleosides are incorporated into DNA in determinable locations, and various diagnostic methods are used to determine the location of the modified nucleosides. These methods include radiolabeling, fluorescent labeling, biotinylation, and strand cleavage. An example of strand cleavage involves reacting the nucleoside with hydrazine to yield urea nucleosides, then reacting the urea nucleoside with piperidine to cause strand cleavage (the Maxam-Gilbert method).

Brief Summary Text (9):
Modifications of nucleosides that have been previously described include 2'-position sugar modifications, 5-position pyrimidine modifications, 8-position purine modifications, modifications at exocyclic amines, substitution of 4-thiouridine, substitution of 5-bromo or 5-iodo-uracil, backbone modifications, and methylations. Modifications have also included 3' and 5' modifications such as capping. PCT WO 91/14696, incorporated herein by reference, describes a method for chemically modifying antisense oligonucleotides to enhance entry into a cell.

Brief Summary Text (12):
RNA has been stabilized against endonucleolytic cleavage by modifying the 2'-

position of the ribonucleosides. One approach to stabilization against base-specific endonucleolytic cleavage rests on the interference with base recognition by enzymes. Several strategies for this modification are known, including modification with 2'-amino and 2'-fluoro (Hobbs et al., Biochemistry, 12:5138 (1973), Guschlbauer et al., Nucleic Acid Res. 4:1933 (1977)), and 2'-OCH.sub.3 (Shibahara et al., 15:4403 (1987); Sproat et al., Nucleic Acids Res., 17:3373 (1989), each of which is hereby incorporated by reference). PCT WO 91/06556, also incorporated by reference, describes nuclease-resistant oligomers with substituents at the 2'-position. PCT WO 91/10671 describes antisense oligonucleotides chemically modified at the 2'-position and containing a reactive portion capable of catalyzing, alkylating, or otherwise affecting the cleavage of RNA, a targeting portion, and a tether portion for connecting the targeting and reactive portions.

Brief Summary Text (19):
The modified purine compounds of the invention are structurally illustrated by formulae (I) and (II) and the modified pyrimidine compounds are structurally illustrated by formulae (III) and (IV), below. The modified urea nucleosides of the present invention are illustrated by formulae (V) and (VI). ##STR1## wherein: X is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, --NR.sup.10.sub.2, and C(O)CH(R.sup.8)C (R.sup.8).sub.2 NR.sup.1 R.sup.2, and wherein at least one of X is C(O)CH(R.sup.8) CH(R.sup.8).sub.2 NR.sup.1 R.sup.2,

Brief Summary Text (20):
R.sup.1 and R.sup.2 are independently selected from the group consisting of H, C.sub.1 -C.sub.18 alkyl, alkenyl or alkynyl, phenyl, aralkyl, alkaryl, an alkanoic acid or its ester and amide derivatives, a peptide fragment which possesses a specified function (i.e., an enzyme inhibitor, receptor antagonist, receptor agonist, etc.), an HIV aspartyl protease inhibitor, groups that are cleaved intracellularly, and groups that increase the hydrophilicity, hydrophobicity, electrostatic capacity or hydrogen bonding capacity of the compound;

Brief Summary Text (23):
R.sup.8 is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, trialkyl silyl, dialkylaryl silyl, alkyldiaryl silyl, triarylsilyl, and --C(O)--R.sup.9, where R.sup.9 is selected from the group consisting of H, alkyl, aryl, aralkyl, alkaryl and alkoxy;

Brief Summary Text (27):
The general process used to prepare the modified purines and pyrimidines is shown below in Scheme I using cytidine and guanine starting materials. As shown in the scheme, the process includes reacting a nucleoside with a suitable leaving group with a palladium catalyst in conjunction with a vinylstannane and carbon monoxide to provide an ene-one functionalized nucleoside intermediate. The intermediate is then reacted with a functionalized amine containing the desired R.sup.1 and R.sup.2 groups in a Michael addition reaction. When primary amines (or secondary amines that contain a cleavable functional group) are added to a pyrimidine ring with an ene-one at the 5-position, the amine is capable of a second Michael addition reaction that adds to the ene-one or ene-imine in the pyrimidine ring. When an ene-one functionality is introduced at the 2-, 6- or 8-position of a purine ring, and a primary amine is added via a Michael addition reaction, the purine ring system is not capable of participating in a second Michael addition reaction. ##STR2##

Brief Summary Text (29):
The intermediate containing the 3-ene-1-one moiety is a key intermediate which can be used to synthesize a number of compounds of the invention. In the case of pyrimidines with a leaving group at the 5-position, treating the intermediate with primary amines (as the free base or as the hydrochloride salt in the presence of an organic base) forms the urea nucleoside derivatives of Formulae V and VI. Alternatively, secondary amines can react with the 3-ene-1-one intermediates to

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give the nucleoside derivatives of Formulae I-IV. The chemistry described in steps a and b is described in U.S. Pat. No. 5,428,149 to Eaton, the contents of which are hereby incorporated by reference.

Brief Summary Text (30):
In one embodiment, the 5'- and 3'-hydroxy groups in nucleoside derivatives with a suitable leaving group at the 5-position can be protected with a tetraisopropyldisiloxyl (TIPS) group to gain access to "free" nucleoside analogs. These compounds undergo the above-described palladium catalyzed conversion in good yield to provide the TIPS protected intermediates.

Brief Summary Text (34):
The nucleosides can also be modified such that they contain one or more radiolabels. Suitable radiolabels include, but are not limited to, .sup.14 C, .sup.32 P, .sup.3 H, .sup.131 I, .sup.35 S, .sup.18 O, and .sup.19 F. These radiolabels can be incorporated into the nucleoside by means known to those of skill in the art. The nucleosides can also contain fluorescent labels, such as rhodamine or fluorescein, and/or can be biotinylated. When modified in this fashion, the nucleosides are particularly useful as in vivo or in vitro diagnostic agents.

Brief Summary Text (39):
As used herein, the term "nucleoside starting material" is defined as any nucleoside base, nucleoside or nucleotide that has an attached acceptable leaving group. Nucleoside starting materials include all nucleosides, both naturally occurring and non-naturally occurring. Preferably, nucleoside starting materials include purines and pyrimidines, which include uracil, thymine, cytosine, adenine, and guanine starting materials. The leaving group can be attached to any free carbon on the nucleoside base. The acceptable leaving group is displaced during the palladium coupling reaction and replaced with an ene-one moiety. The resulting intermediate is reacted with a suitable amine to provide the modified nucleosides of the present invention.

Brief Summary Text (40):
As used herein, the term "pyrimidine starting material" is defined as a pyrimidine base, pyrimidine nucleoside or pyrimidine nucleotide that has an attached acceptable leaving group. Pyrimidine starting materials include all pyrimidines, both naturally occurring and non-naturally occurring. Preferably, pyrimidine starting materials include uracil, thymine, and cytosine with attached leaving groups. The leaving group can be attached to any free carbon on the nucleoside, preferably at the 5- or 6-position. The most preferred attachment is at the 5-position.

Brief Summary Text (41):
As used herein, the term "purine starting material" is defined as a purine base, purine nucleoside or purine nucleotide that has an attached acceptable leaving group. Purine starting materials include all purines, both naturally occurring and non-naturally occurring. Preferably, purine starting materials include adenine and guanine with attached leaving groups. The leaving group can be attached to any free carbon on the nucleoside, preferably at the 2-, 6-or 8-position. The most preferred attachment is at the 8-position.

Brief Summary Text (42):
As used herein, the term "palladium catalyst" is defined as any palladium catalyst capable of coupling a purine or pyrimidine ring, a vinyl stannane and carbon monoxide to form an ene-one modified purine or pyrimidine nucleoside. Suitable catalysts for performing the coupling reaction include, but are not limited to PdL.sub.3 and PdL.sub.4 where L is any ligand normally associated with palladium. The preferred catalyst for the coupling reaction is Pd[P(Ph).sub.3].sub.3. Catalysts including mixtures of Pd[P(Ph).sub.3].sub.3 and Pd(OAc).sub.2 are also

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suitable for practicing the present invention. When Pd(P(Ph).sub.3).sub.3 and Pd (OAc).sub.2 are employed together, the preferred molar ratio is about 3:1 Pd(P (Ph).sub.3).sub.3 to Pd(OAc).sub.2. In a preferred embodiment, the catalyst also includes CuI.

Brief Summary Text (46):
As used herein, the term "alkynyl" is defined as a C.sub.2-18 straight or branched alkene, or a C.sub.8-18 cyclic alkene. Preferably, the alkynyl groups are between C.sub.2 and C.sub.10, and, more preferably, between C.sub.2 and C.sub.6.

Brief Summary Text (55):
As used herein, the term "modified nucleoside" is defined as a non-naturally occurring nucleoside, and specifically includes uridine, cytidine, adenine and guanine derivatives, as well as the urea nucleoside derivatives. The modified nucleosides of the present invention include at least one moiety of the formula C (O)CH(R.sup.8)C(R.sup.8).sub.2 NR.sup.1 R.sup.2, where R.sup.1, R.sup.2 and R.sup.8 are as defined below.

Brief Summary Text (56):
As used herein, the term "vinylstannane" is defined as (alkyl.sub.3 Sn)(R.sup.8) C.dbd.C(R.sup.8).sub.2, wherein alkyl is preferably n-butyl, and R.sup.8 is, independently, selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, trialkyl silyl, dialkylaryl silyl, alkyldiaryl silyl, triarylsilyl, and --C(O)--R.sup.9, where R.sup.9 is selected from the group consisting of H, alkyl, aryl, aralkyl, alkaryl and alkoxy.

Brief Summary Text (67):
Modified nucleosides and methods of preparation and use thereof are disclosed. The modified nucleosides have the general formulae: ##STR5## wherein: X is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, --NR.sup.10.sub.2, and C(O)CH(R.sup.8)C (R.sup.8).sub.2 NR.sup.1 R.sup.2, and wherein at least one of X is C(O)CH(R.sup.8)C (R.sup.8).sub.2 NR.sup.1 R.sup.2,

Brief Summary Text (68):
R.sup.1 and R.sup.2 are independently selected from the group consisting of H, C.sub.1 -C.sub.18 alkyl, alkenyl or alkynyl, phenyl, aralkyl, alkaryl, an alkanoic acid or its ester and amide derivatives, a peptide fragment which possesses a specified function (i.e., an enzyme inhibitor, receptor antagonist, receptor agonist, etc.), an HIV aspartyl protease inhibitor, groups that are cleaved intracellularly, and groups that increase the hydrophilicity, hydrophobicity, electrostatic capacity or hydrogen bonding capacity of the compound,

Brief Summary Text (71):
R.sup.8 is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, trialkyl silyl, dialkylaryl silyl, alkyldiaryl silyl, triarylsilyl, and --C(O)--R.sup.9, where R.sup.9 is selected from the group consisting of H, alkyl, aryl, aralkyl, alkaryl and alkoxy;

Brief Summary Text (75):
The nucleosides can also be modified such that they contain one or more radiolabels. Suitable radiolabels include, but are not limited to, .sup.14 C, .sup.32 P, .sup.3 H, .sup.131 I, .sup.35 S, .sup.18 O, and .sup.19 F. These radiolabels can be incorporated into the nucleoside by means known to those of skill in the art. The nucleosides can also contain fluorescent labels, such as rhodamine or fluorescein, or can be biotinylated. These labels can be incorporated into the nucleoside by means known to those of skill in the art. When modified in this fashion, the nucleosides are particularly useful as in vivo or in vitro diagnostics.

Brief Summary Text (78):
a) optionally protecting one or more of the hydroxy groups in a nucleoside starting material that contains the desired R.sup.3-6 groups,

Brief Summary Text (79):
b) reacting the nucleoside starting material containing a leaving group attached to a carbon of the nucleoside starting material with a suitably substituted vinylstannane or other suitable compound and carbon monoxide in the presence of a palladium catalyst to replace the leaving group with a 3-ene-1-one moiety, and

Brief Summary Text (81):
Preparing Nucleoside Derivatives with the Desired R.sup.3-6 groups

Brief Summary Text (82):
Preparation of modified nucleosides in general, and cytidine, uridine, guanine and adenine derivatives, in particular, is well known. Modifications of nucleosides that have been previously described include 2'-position sugar modifications, 5'-position pyrimidine modifications, 8-position purine modifications, modifications at exocyclic amines, substitution of 4-thiouridine, substitution of 5-bromo or 5-iodo-uracil, backbone modifications, and methylations. Modifications have also included 3' and 5' modifications such as capping. PCT WO 91/14696 describes a method for chemically modifying antisense oligonucleotides to enhance entry into a cell.

Brief Summary Text (83):
The modified nucleosides can be prepared by means well known to those of skill in the art. A straightforward method for modifying nucleosides at the 2'-position involves protecting reactive functional groups on the base, and protecting the 3'- and 5'-hydroxy groups as the TIPS ethers. This allows functionalization of the 2'-hydroxy group using known chemistry that does not adversely affect the protecting groups. For example, the 2'-hydroxy group in a suitably protected nucleoside can be reacted with methyl iodide to form a methyl ether. Reaction with tosyl chloride or a similar compound to convert the hydroxy group to a suitable leaving group, followed by nucleophilic displacement with a desired nucleophile, can also provide a variety of substitutions at the 2'-position.

Brief Summary Text (87):
The palladium coupling chemistry in step b) of the synthesis is described in detail in U.S. Pat. No. 5,428,149 to Eaton. Briefly, the hydroxy groups on a nucleoside starting material are optionally protected. The protected or unprotected nucleoside starting material is combined with a vinylstannane or other suitable compound and carbon monoxide in the presence of a suitable palladium catalyst.

Brief Summary Text (88):
Halogen leaving groups, particularly iodo or bromo derivatives, are preferred for the coupling chemistry. However, nucleoside derivatives with other leaving groups, such as trifluoroacetate, tifluoromethyl sulfonate, and boronic acids and ester derivatives can be used.

Brief Summary Text (93):
In an alternative embodiment, the hydroxy groups in the desired nucleoside derivatives can be protected with a tetraisopropyldisiloxyl (TIPS) group to gain access to "free" nucleoside analogs. These compounds undergo the above-described palladium catalyzed conversion in good yield to provide the TIPS protected intermediates.

Brief Summary Text (99):
Interestingly, it has been observed that when pyrimidine nucleosides are modified in the 5-position with the ene-one moiety, and a primary amine is added to the ene-one in a first Michael addition reaction, a second Michael addition reaction with

the ene-one or ene-imine in the pyrimidine ring is possible. Accordingly, the 5-position modified pyrimidine intermediate from the palladium coupling chemistry (step b) described above can be reacted with primary amines (as the free base or as the hydrochloride salt in the presence of an organic base) in a double Michael reaction to form urea nucleoside derivatives.

Brief Summary Text (103):
Representative modified nucleoside compounds of the present invention are shown in Tables I and II. Table I exemplifies compounds of the formula (III) wherein R.sup.1 -R.sup.6 have the values indicated. Table II exemplifies compounds of the formula (V) wherein R.sup.1 -R.sup.6 have the values indicated. These compounds can be converted to the corresponding cytidine derivatives (of Formulae IV and VI, respectively) using known methods.

Brief Summary Text (104):
Specific non-limiting examples of the synthesis of modified nucleoside compounds of the present invention are illustrated below in Schemes II and III. For example, commercially available 5-iodouridine can be protected as the isopropylidene 1 which can then be treated with vinyltributyltin and carbon monoxide in the presence of a palladium catalyst to give 2 in high yield (Scheme 11). Compound 2 is a key intermediate which can be used to synthesize a number of compounds of the invention. Treatment of 2 with primary amines (as the free base or as the hydrochloride salt in the presence of an organic base) leads to the formation of the urea nucleoside derivatives 3-7. The amine hydrochloride (or any other salt) can be used directly in the presence of an organic base such as triethylamine or, the free base of the amine can be generated separately by treating the amine salt with CaH.sub.2 in DMF. Alternatively, secondary amines can be utilized to react with 2 to give the uridine derivatives 8-11.

Brief Summary Text (105):
Protection of 5-iodouridine with the tetraisopropyldisiloxyl (TIPS) group can be utilized to gain access to the "free" nucleoside analogs (Scheme III). Treatment of 5-iodouridine with dichloro-tetraisopropyldisiloxane in DMF in the presence of imidazole provides the 3',-5'-TIPS derivative 12. Compound 12 undergoes the palladium catalyzed conversion in good yield to provide the TIPS protected intermediate 13. Reaction of 13 with primary amines gives the secondary amines 14-15 which can be deprotected with polymer-supported fluoride to provide the nucleosides 16-17. The derivatives 16-17 rearrange slowly to 18-19 upon treatment with triethylamine in DMSO. Compounds 18-19 can be synthesized directly from 14-15 by deprotection with triethylamine hydrofluoride effecting deprotection and rearrangement in one step. The intermediate 13 can be converted to the uridine analog 20-21 in the presence of secondary amines in a manner analogous to the previously described reactions of isopropylidene 2. Deprotection of 20-21 with either HF/triethylamine of polymer-supported fluoride provides the nucleosides 22-23 in high yield. It will be evident to those skilled in the art that each of the above mentioned reactions may require slightly different reaction and purification conditions in order to obtain optimized yields of the desired products.

Brief Summary Text (109):
Several nucleosides are known to possess anti-viral activity. These are often modified nucleosides, where the modification is at the 2' or 3' positions. Modified nucleosides can inhibit viral replication by inhibiting viral thymidine kinase by slowing replication. Replication is slowed by reducing the amount of nucleotide monophosphates available. Alternatively, nucleoside analogs like acyclovir take advantage of the different specificity of the thymidine kinases, viral and human, by only being phosphorylated by the viral enzyme. The phosphorylated nucleoside is subsequently incorporated by the infected cells, resulting in chain termination and cell death. The nucleosides of the present invention can be modified to be phosphorylated by viral kinases, in preference to the human kinases, leading to specificity and reduced toxicity.

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Brief Summary Text (110):
Modifications that result in increased specificity to viral kinases are well known to those of skill in the art. For example, the 3' position can be modified to contain an azide moiety, as in AZT. By incorporating known modifications to the nucleosides at the 2' and 3' positions (R.sup.3 -R.sup.5), the modified nucleosides of the present invention are expected to also have anti-viral activity. In addition, modifying R.sup.1 and R.sup.2 on the amine can also provide anti-viral activity. For example, R.sup.2 can be a proteinase inhibitor, and R.sup.5 can be an azide, to provide a dual activity anti-viral compound. Alternatively, R.sup.2 can be a moiety that is cleaved intracellularly, such that the virus incorporates the nucleoside, and when the moiety is cleaved intracellularly, the modified nucleoside disrupts viral replication. Methods for screening anti-viral activity are well known to those of skill in the art.

Brief Summary Text (113):
When administered as anti-cancer, anti-bacterial or antiviral drugs, the compounds can be administered in a range of between approximately 0.5-98 mg nucleoside/m.sup.2 /day, preferably between 15 and 25 mg nucleoside/m.sup.2 /day. Preferred modes of administration include parental, intravenous, intramuscular, and oral. When administered via injection, the nucleosides can be dissolved in a pharmaceutically acceptable carrier, such as PBS, saline, and dextrose solutions. Typical concentrations range from between approximately 0.5 to 50 mg/mL solution, and more preferably, between approximately 1.0-25 mg/mL solution. The amount of nucleoside administered to a patient will be expected to vary according to the nature and severity of the disease to be treated, as will be judged by a physician of skill in the art.

Brief Summary Text (118):
When the nucleosides contain a radiolabel, a fluorescent tag such as rhodamine or fluorescein, are biotinylated, they can be detected after the nucleoside is incorporated into DNA. These embodiments are particularly useful as in vivo or in vitro diagnostics. Oligonucleotides that include the modified nucleosides can also be labeled, and when they specifically bind to or interact with a target site, the binding or interaction can be observed by detecting the label. This can be useful as a diagnostic tool, to determine whether a particular binding site is present in a sample by adding a specific oligonucleotide that selectively binds to or interacts with the site, washing away unbound oligonucleotide, and observing binding or interaction by looking for the label.

Brief Summary Text (121):
The compounds of the invention are useful as strand cleavage reagents for sequencing oligonuclcotides. The triphosphates of the 5-[(R.sup.1 R.sup.2) aminoethylcarbonyl]pyrimidine nucleosides (where one of R.sup.1 or R.sup.2 is a protective group which masks the amino group) are incorporated into DNA and/or RNA during enzyme catalyzed polymerase reactions. The full length oligonucleotide is then exposed to a reagent which removes the amine protective group thereby unmasking the amine. The intramolecular Michael addition reaction leads to the formation of a urea nucleoside derivative which is formally related to the urea nucleoside obtained from exposure of thymidine to hydrazine in the Maxam-Gilbert sequencing method. The urea nucleoside is then cleaved with piperidine which leads to strand cleavage via the known .beta.-elimination mechanism of the Maxam-Gilbert method (Scheme IV). The compounds of the invention may be useful for cleaving large oligonucleotides into smaller fragments for sequencing or use in gene shuffling applications. ##STR11##

US Reference Patentee Name (8):
Hobbs, Jr. et al.

US Reference Group (8):

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5047519 19910900 Hobbs, Jr. et al.

Other Reference Publication (35):
Hobbs et al. (1973) Biochem. 12:5138.

CLAIMS:

1. A compound selected from the group consisting of ##STR12## wherein: X is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy, --NR.sup.10.sub.2, and --C(O)CH(R.sup.8)C (R.sup.8).sub.2 NR.sup.1 R, and wherein at least one of X is --C(O)CH(R.sup.8)C (R.sup.8).sub.2 NR.sup.1 R;

R.sup.1 and R.sup.2 are independently selected from the group consisting of H, C.sub.1 -C.sub.18 alkyl, alkenyl or alkynyl, phenyl, aralkyl, alkaryl, an ester or amide derivative of an alkanoic acid, a peptide fragment, an HIV aspartyl protease inhibitor, a group that is cleaved intracellularly, and a group that increases the hydrophilicity or hydrophobicity of the compound;

R.sup.3 is H;

R.sup.4 and R.sup.5 are independently selected from the group consisting of H, --OH, protected oxy-, NH.sub.2, F, N.sub.3, --CN, --NC, --OAC, --Sac, --OBz and --OSiR.sup.7.sub.3, wherein R.sup.7 is C.sub.1 -C.sub.4 alkyl or phenyl;

R.sup.6 is selected from the group consisting of --OH, protected oxy-, phosphate, diphosphate, triphosphate, phosphate ester, phosphoramidite, phosphorothionate and phosphorodithionate;

R.sup.9 is independently selected from the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl, alkoxy and --C(O)--R.sup.9, where R.sup.9 is selected form the group consisting of H, aryl, aralkyl, alkyl, alkaryl, alkenyl, alkynyl and alkoxy;

R.sup.10 is independently selected from the group consisting of H, alkyl, aryl, aralkyl, alkaryl, and R.sup.9 C(O);

the protected oxy- groups R.sup.4 and R.sup.5 taken together represent an isopropylidene group of the formula --OC(CH.sub.3).sub.2 O-- or an orthoformate group of the formula --OCH(OR.sup.7)O--; and

the protected oxy- groups of the R.sup.4 and R.sup.5 taken together can represent a 3'-5'-tetraalkyldisiloxane group of the formula --OS(alkyl).sub.2 OSi(alkyl).sub.2 O--;

wherein said compound is optionally modified with a label selected from the group consisting of radiolabels and fluorescent labels.

First Hit Fwd Refs

L5: Entry 4 of 5 File: USPT Oct 20, 1998

US-PAT-NO: 5824796
DOCUMENT-IDENTIFIER: US 5824796 A

TITLE: Cross-linking oligonucleotides

DATE-ISSUED: October 20, 1998

INVENTOR-INFORMATION:

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APPL-NO: 08/ 334490 [PALM]
DATE FILED: November 4, 1994

PARENT-CASE:
CROSS REFERENCE TO RELATED APPLICATIONS This application is a continuation of application Ser. No. 08/049,807, filed Apr. 20, 1993, now abandoned which is in turn a continuation of application Ser. No. 07/353,857, filed May 18, 1989, now abandoned, which in turn is a continuation-in-part of application Ser. No. 250,474, filed on Sep. 28, 1988.

INT-CL: [06] C07 H 19/04, C07 H 21/00, C07 H 21/02, C07 H 21/04

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US-CL-CURRENT: 536/26.7; 536/24.5

FIELD-OF-SEARCH: 536/26.1, 536/26.12, 536/26.13, 536/26.14, 536/26.8, 536/27.6, 536/27.81, 536/28.5, 536/28.54, 536/26.7, 536/24.5

PRIOR-ART-DISCLOSED:

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Search Selected Search ALL Clear

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ART-UNIT: 121

PRIMARY-EXAMINER: Kunz; Gary L.

ATTY-AGENT-FIRM: Klein & Szekeres, LLP

ABSTRACT:

This invention is directed to novel substituted nucleotide bases with a crosslinking arm which accomplish crosslinking between specific sites on adjoining strands of oligonucleotides or oligodeoxynucleotides. The invention is also directed to oligonucleotides comprising at least one of these crosslinking agents and to the use of the resulting novel oligonucleotides for diagnostic and therapeutic purposes. The crosslinking agents of the invention are of the following formula (I'):

R.sub.1 --B--(CH.sub.2).sub.q --(Y).sub.r --(CH.sub.2).sub.m --A'(I')

wherein,

R.sub.1 is hydrogen, or a sugar moiety or analog thereof optionally substituted at its 3' or its 5' position with a phosphorus derivative attached to the sugar moiety by an oxygen and including groups Q.sub.1 Q.sub.2 and Q.sub.3 or with a reactive precursor thereof suitable for nucleotide bond formation;

Q.sub.1 is hydroxy, phosphate or diphosphate;

Q.sub.2 is .dbd.O or .dbd.S;

Q.sub.3 is CH.sub.2 --R', S--R', O--R', or N--R'R";

each of R' and R" is independently hydrogen or C.sub.1-6 alkyl;

B is a nucleic acid base or analog thereof that is a component of an oligonucleotide;

Y is a functional linking group;

each of m and q is independently 0 to 8, inclusive;

r is 0 or 1; and

A' is a leaving group.

This invention is also directed to novel 3,4-disubstituted and 3,4,-trisubstituted pyrazolo[3,4-d]-pyrimidines and to the use of these nucleic acid bases in the

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preparation of oligonucleotides. The invention includes nucleosides and mono- and oligonucleotides comprising at least one of these pyrazolopyrimidines, and to the use of the resulting novel oligonucleotides for diagnostic purposes.

15 Claims, 3 Drawing figures

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First Hit Fwd Refs

L5: Entry 4 of 5 File: USPT Oct 20, 1998

DOCUMENT-IDENTIFIER: US 5824796 A
TITLE: Cross-linking oligonucleotides

Brief Summary Text (2):
This invention relates to nucleoside crosslinking agents and to the use of these compounds in the preparation of oligonucleotides. It also relates to derivatives of pyrazolo[3,4-d]pyrimidine which are useful as nucleic acid bases for the preparation of oligonucleotides.

Brief Summary Text (3):
Oligonucleotides are useful as diagnostic probes for the detection of "target" DNA or RNA sequences. In the past, such probes were made up of sequences of nucleic acid containing purine, pyrimidine or 7-deazapurine nucleotide bases (U.S. Pat. No. 4,711,955; Robins et al., J. Can. J. Chem., 60:554 (1982); Robins et al., J. Org. Chem., 48:1854 (1983)). The method for attaching chemical moieties to these bases has been via an acetoxy-mercuration reaction, which introduces covalently bound mercury atoms into the 5-position of the pyrimidine ring, the C-8 position of the purine ring or the C-7 position of a 7-deazapurine ring (Dale et al., Proc. Natl. Acad. Sci. USA, 70:2238 (1973); Dale et al., Biochemistry, 14:2447 (1975)), or by the reaction of organomercurial compounds with olefinic compounds in the presence of palladium catalysts (Ruth et al., J. Org. Chem., 43:2870 (1978); Bergstrom et al., J. Am. Chem. Soc., 100:8106 (1978); Bigge et al., J. Am. Chem. Soc., 102:2033 (1980)).

Brief Summary Text (5):
A novel class of nucleotide base, the 3,4-disubstituted and 3,4,6-trisubstituted pyrazolo[3,4-d]-pyrimidines, has now been found which offers several advantages over the prior art. The de novo chemical synthesis of the pyrazolopyrimidine and the resulting nucleotide allows for the incorporation of a wide range of functional groups in a variety of different positions on the nucleotide base and for the use of different sugar moieties. Also, adenine, guanine and hypoxanthine analogs are obtained from a single nucleoside precursor. Additionally, the synthesis does not require the use of toxic heavy metals or expensive catalysts. Similar pyrazolo[3,4-d]pyrimidines are known (Kobayashi, Chem. Pharm. Bull., 21:941 (1973)); however, the substituents on the group are different from those of the present invention and their only use is as xanthine oxidase inhibitors The concept of crosslinkable nucleotide probes for use in therapeutic and diagnostic applications is related to the pioneering work of B. R. Baker, "Design of Active-Site-Directed Irreversible Enzyme Inhibitors," Wiley, N.Y., (1967), who used what was termed "active-site-directed enzyme inhibitors" in chemotherapeutic applications.

Drawing Description Text (30):
For example, the general procedure of Robins et al. (J. Can. J. Chem., 60:554 (1982); J. Org. Chem., 48:1854 (1983)) may be adapted, as shown in Scheme 1, to the palladium-mediated coupling of a substituted 1-alkyne (XXI) to 5-iodo-2'-deoxyuridine (XX) to give the acetylene-coupled product (XXII). The acetylenic dUrd analog XXII is reduced, with Raney nickel for example, to give the saturated compound (XXIII), which is then used for direct conversion to a reagent for use on an automated DNA synthesizer, as described below. ##STR3##

Drawing Description Text (31):

h e b b g e e e f e e e f

When 5-chloromercurio-2'-deoxyuridine (XXIV) is used as a starting compound, it cannot be directly coupled to an olefin group to give the olefinic compound (XXVII) by palladium-catalyzed coupling with functionalized olefins. Instead, as shown in Scheme 2, a substituted alkene (XXV) and 5-chloromercurio-2'-deoxyuridine (XXIV) are reacted together with methanol to give the alpha-methoxy adduct (XXVI), which is converted to the olefinic compound XXVII by trifluoroacetic acid and trifluoroacetic anhydride. Reduction gives the saturated compound (XXIII), to be converted to the DNA synthesizer-ready reagent as described below.

Drawing Description Text (32):
The second class of modified nucleoside is a group of 2'-deoxy-4-aminopyrazolo[3,4-d]pyrimidine derivatives. The general structure of these derivatives is presented below: ##STR4##

Drawing Description Text (46):
The synthesis of 3,4-disubstituted and 3,4,6-trisubstituted pyrazolo[3,4-d] pyrimidine nucleosides and their use as reagents for incorporation into nucleic acids either enzymatically or via chemical synthesis offers several advantages over current procedures. The de novo chemical synthesis of the nucleotide allows for the incorporation of a wide range of functional groups (e.g., NH.sub.21 SH, OH, halogen, COOH, CN, CONH.sub.2) and the use of different sugar moieties. Also, adenine, guanine, and hypoxanthine analogs are obtained from a single nucleoside precursor. And, the synthesis does not require the use of toxic heavy metals or expensive catalysts.

Detailed Description Text (27):
The monophosphate of Example 8 (80 mg, ca. 0.1 mmole) was dissolved in DMF with the addition of triethylamine (14 .mu.L). Carbonyldiimidazole (81 mg, 0.5 mmole) was added and the solution stirred at RT for 18 hr. The solution was treated with methanol (40 .mu.L), and after stirring for 30 min tributylammonium pyrophosphate (0.5 g in 0.5 mL DMF) was added. After stirring for 24 hr another aliquot of tributylammonium pyrophosphate was added and the solution was stirred overnight. The reaction mixture was evaporated to dryness and chromatographed following the procedure in Example 8. Two products were collected and were each separately treated with conc. ammonium hydroxide (1 mL) for 18 hr at 55.degree. C. UV and HPLC analysis indicated that both products were identical after ammonia treatment and were pooled and lyophilized to give 35.2 mg of nucleoside triphosphate.

Detailed Description Text (68):
The compound of Example 17 is reacted with dimethoxytrityl chloride and pyridine to give the corresponding 5'-dimethoxytrityl compound. This compound is then reacted with cyanoethyl chloro-N,N-diisopropyl- phosphoramidite (according to the method of Sinha et al., Nucleic Acids Res., 12:4539 (1984)) to give the 3'-O-activated nucleoside.

Detailed Description Text (86):
Following the above procedures, the nucleoside 5-(3-trifluoroacetamidoprop-1-yl)-2'-deoxyuridine was converted to the 5'-O -dimethoxytrityl-3'-(N,N-diisopropyl) -phosphoramidite cyanoethyl ester derivative. This was added to a DNA synthesizer and the following 14-mer oligonucleotide sequence was prepared: